COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES

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BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled ***"COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES"*** is the original and bonafide work done by **Dr.S.PRAKASAM** under the guidance of **Prof.Dr.D.ANURADHA, M.D.,DCH.,** Professor , Department of Pediatrics , GovernmentKilpauk Medical College & Hospital, Chennai – 600 010, during the tenure of his course in M.D. Pediatrics from May-2016 to May-2019 held under the rules and regulations of the Tamilnadu Dr. M.G.R Medical University, Guindy, Chennai – 600 032,in partial fulfilment for the award of the degree of M.D Branch VII Paediatrics.

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This is to certify that this dissertation titled ***"COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES"*** is the original and bonafide work done by **Dr.S.PRAKASAM** under my guidance and supervision at Government Kilpauk Medical College & Hospital, Chennai – 600 010, during the tenure of his course in M.D. Pediatrics from May-2016 to May-2019 held under the university rules and regulations of The Tamilnadu Dr.M.G.R. Medical University, Guindy , Chennai – 600 032, in partial fulfilment for the award of the degree of M.D Branch VII Paediatrics.

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I solemnly declare that this dissertation titled ***"COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES"*** is the original and bonafide work done by me at the Government Kilpauk Medical College & Hospital, Chennai – 600 010, under the guidance and supervision of **Prof.Dr.D.ANURADHA, M.D.,DCH.,** Professor , Department of Pediatrics , Government Kilpauk Medical College & Hospital, Chennai – 600 010.

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This is to certify that this dissertation work titled ***"COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES"***of the candidate **Dr.S.PRAKASAM,** Post graduate in **PAEDIATRICS** with registration Number **201617151** for the award of **M.D.PAEDIATRICS** in the **Branch VII**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **8%** percentage of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION

Cardio vascular diseases mainly ischaemic heart diseases and stroke are the leading causes of death in world.

The genetic and lifestyle risk factors of these diseases are well known and include hypercholesterolemia, hypertension, smoking, obesity and inadequate physical activity.

Atherosclerotic cardiovascular diseases is a major cause for morbidity and mortality in adult population.

Hyperlipidemia may cause complications such as stroke, kidney failure, coronary artery diseases.

Altered lipid levels was the well known factor in coronary heart diseases and this process is considered to begin in early life and progressed silently over decades.

In the 1980^s English physician and epidemiologist David Barker of the university of Southampton formulated a hypothesis stating that the intrauterine environment influences the patterns of physiological process in the foetus that in certain conditions may influence the presence of medical disorders in future life.

Barker et al demonstrated that low birth weight is correlated with increased prevalence of cardio vascular diseases in future.

He analysed data from Hertfordshire, concerning the birth weight of all new borns from 1911 and their development through the infancy

period, barker noted that over a period of 60 years the people whose birth weight was higher at birth had lower mortality from cardiovascular diseases.

This was in synchronization with foetal origin hypothesis and reflects the phenomenon that programming whereby a stimulation or any insult during critical period of intrauterine life could result in alternation of physiology and metabolism during adult life.

Studies in human have shown that men and women with low birth weight are at increased risk of coronary artery heart diseases.

Human foetuses are known to permanently change their physiology and metabolism to adapt to limited supply of nutrients inutero.

Concentrations of cord blood lipoproteins levels are influenced by foetal malnutrition and prematurity.

These programmed changes can later be the cause for the origin of diseases like coronary artery diseases, hypertension and diabetes mellitus.

It is well documented that atherosclerosis starts in childhood and there is evidence that this association with adult level may originate at birth, so assessment of serum lipid levels in neonates might be of importance.

Abnormal lipoprotein profile in newborn may persist into adult life so young age can be viewed as an opportunity to begin preventable interventions to change risk factors for cardiovascular diseases.

Hence this study will be conducted to compare umbilical cord blood lipid profile between normal and low birth weight babies.

High concentrations of triglycerides rich lipoproteins are seen with infants with low birth weight. A study done by Dr. Anomika gora, Dr. Plak gupta, Dr.M.L. Gupta. Scholar journal of applied medical sciences. Sch J.App Med Sci 2017 ;5(7c): 2662- 2665.

Many studies have confirmed the importance of proper intrauterine development and all the factors that affect it will affect the future life.

Donega et al reported that the concentration of total cholesterol, LDL, HDL, apolipoproteins were higher in preterm than in term babies. whereas triglycerides level will be higher in preterm babies than in term babies.

Therefore it is reasonable to search for the first risk factors of life style diseases as early as possible in the neonatal period.

The aim of this study is to examine the possible relationships among several foetal and maternal factors and the neonatal cord blood lipid profile inorder to detect any possible characteristics that may predispose neonates to higher risk of coronary heart diseases in future.

There are a number of maternal as well as fetal high risk factors, which adversely affect the fetal-placental unit, thus compromising its functions. Some of the well recognized maternal as well as fetal factors are pregnancy induced hypertension, chronic maternal diseases like diabetes mellitus hypertension etc, ante-partum hemorrhage, prolonged labour, premature rupture of membranes (more than 12 hours),fetal

distress due various causes ,cord compression and low apgar score, low birth weight and prematurity.

Although blood cholesterol and lipid profile have been extensively studied in adults, limited studies are available in pediatric population, more so in our country. There is scanty data on serum lipid levels in preterm and term newborns. This study was undertaken to find out the influence of prematurity on cord lipid levels and to compare the cord blood lipid levels in term and preterm newborns.[12]

Lipid profile is a marker of an underlying cardiovascular status. Lipid profile includes measurement of cholesterol and its derivatives and various atherogenic indices. Studies have shown that SGA babies had abnormal lipid profile compared to AGA babies.[8, 9, 10, 11,12]

There are many studies showing the direct relationship between the abnormalities in lipid profile among the SGA babies and occurrence of cardiovascular diseases. The present study was undertaken for early detection of abnormalities in the lipid profile at the earliest (at birth), especially in the Preterm and SGA babies, so that these high risk babies can be under vigilant monitoring in future.

Early diagnosis followed by prudent dietary supplementation and drug therapy in these high risk neonates may provide an opportunity for long range primary amelioration of risk factors that contribute to development of cardio vascular diseases in adult life.

AIMS AND OBJECTIVES

1. To estimate and compare cord lipid profile (total cholesterol [TC], triglyceride [TG], high density lipoprotein [HDL], low density lipoprotein [LDL], (VLDL) (very low density lipoprotein) in normal and low birth weight neonates.
2. Among low birth weight babies to estimate and compare cord lipid profile (total cholesterol [TC], triglyceride [TG], high density lipoprotein [HDL], low density lipoprotein [LDL], very low density lipoprotein[VLDL] in between AGA and SGA neonates.
3. To estimate and compare cord lipid profile (total cholesterol [TC], triglyceride [TG], high density lipoprotein [HDL], low density lipoprotein [LDL], very low density lipoprotein[VLDL] in between boy and girl neonates.
4. To estimate and compare cord lipid profile (total cholesterol [TC], triglyceride [TG], high density lipoprotein [HDL], low density lipoprotein [LDL], very low density lipoprotein[VLDL] in between babies born with primi and multi gravid mothers.

REVIEW OF LITERATURE

Daniel M. Lane et al. studied the various factors affecting the lipid and apolipoprotein levels (A I, A II, C I, C II, C III, Apo B, Apo D and Apo E) in cord sera and they collected data on cord sera levels from the infants whose lipid metabolism might have been modified by a variety of factors present before, at or after delivery. Method of delivery had a little effect except in relation to either fetal immaturity (increased total cholesterol) or fetal stress (increased triglycerides). Birth weight was related to changes in free cholesterol, C I, CIII, and Apo E levels. Gestational age had greater impact upon both serum lipids and apolipoproteins, with increasing fetal maturity, total cholesterol, free cholesterol, AII, C II, Apo E progressively decreased whereas triglyceride and Apo D increased.[13]

P.K.Misra et al have observed a low mean triglyceride and Free Fattyacids (FFA) levels in the cord blood of preterm (28 to 32 weeks) neonates compared to term AGA neonates.[14]

N.Haridas, P.T.Acharya in a study of serum lipid status in neonates carried out serial longitudinal determinations of serum triglycerides, cholesterol, total lipids and lipoproteins in 60 each of normal full term, preterm and low birth weight infants along with maternal triglyceride, cholesterol and total lipid. They found that preterm and low birth weight babies had higher cord blood triglyceride as compared to maternal levels. Alpha lipoproteins constituted a higher percent of total lipoproteins in the cord blood than in the mother's blood. The cholesterol levels were not significantly different in the three groups at birth.[15]

P P Mathur et al in their study on cord blood cholesterol in term and preterm new born found a positive correlation between cord blood cholesterol levels and gestational age, birth weight. Sex of babies did not influence the cholesterol values.

A Kalra et al in their study on serum lipid profile in term and pre term infants showed that total lipids, cholesterol, phospholipids, HDL and LDL were lower in the cord blood of pre term babies as compared to full term babies. But the difference was statistically significant only for total lipids, cholesterol and phospholipids.[17]

J.Dogra et al studied the serum lipid profile of neonatal cord blood in the families affected with diabetes mellitus type I, in 30 full term neonates, and compared them with 30 control neonates without any adverse factors. They found that neonatal triglyceride and cholesterol were present in smaller proportions in cord serum than the maternal serum at the time of parturition and they have different chemical identity from the respective maternal lipids. The difference in serum cholesterol levels in the study and control group was significant, while that of serum triglycerides was insignificant.[18]

Ajay Kumar et al in their study demonstrated that cord blood. Cholesterol levels are not influenced by birth weight and gestation, but levels of cord blood triglyceride and FFA are affected by birth weight and gestation.[19]

Y T Van-der schouw et al in their study of fatty acids composition of serum lipids of mothers and their babies after normal and hypertensive pregnancies suggested that neonatal Essential fatty acids (EFA) status after pregnancy induced hypertension only slightly differs from normal.[20]

Kherkeulidze P et al in their study of HDL particle size distribution in cord blood suggested that irrespective of sex, gestational age and birth weight the newborns had 2 typical HDL subclass distributions, characterized by high or low levels of HDL2b and HDL2a. The newborns with high HDL2b and HDL2a levels also had low VLDL lipid levels and high HDL cholesterol concentrations.[21]

MR Averna et al. studied the prevalence of hypercholesterolemia in cord blood. Cholesterol, triglycerides, HDL cholesterol, apoprotein B and LDL cholesterol in cord blood were assayed. 1275 term newborns were studied. In 3.13% of them cholesterol levels >mean + 2 standard deviations were present. Only 0.47% showed all three parameters levels higher than mean + 2 standard deviations, and 0.31%, in spite of normal cholesterol levels presented high LDL cholesterol and apo B levels. Thus integrated utilization of these parameters in the neonatal screening of familial hypercholesterolemia will have to be confirmed by follow up studies.[22]

Xinli Wang et al. studied the Glucose and Lipid metabolism in Small for gestational age infants at 72 Hours of Age, enrolling 296 singleton neonates (177 males and 119 females), including 76 classified

as small for gestational age (SGA) babies (37 preterm and 39 full term newborns) and 220 appropriate for gestational age (AGA) babies (84 preterm and 136 full-term newborns) were included. Plasma glucose levels were similar in the SGA and AGA groups, both for full-term and preterm infants; however, insulin levels and insulin-to-glucose ratios were significantly higher in the SGA group than in the AGA group. SGA neonates had higher triglyceride, total cholesterol, and LDL-c levels than did AGA infants both among full-term and preterm neonates (triglyceride value 2.29 ± 0.23 vs. 1.57 ± 0.13 mmol/liter in full-term, $P < 0.01$; 2.27 ±0.16 vs. 1.34 ± 0.11 mmol/liter in preterm, $P< 0.01$, total cholesterol value 2.35 ±0.12 vs. 1.82 ± 0.22 mmol/liter in full-term, $P=0.04$; 2.57 ± 0.22 vs. 1.95 ± 0.15 mmol/liter in preterm, $P =0.02$, and LDL-c value 2.11 ± 0.58 vs. 1.24 ±0.61 mmol/ liter in full-term, $P = 0.01$; 1.87 ± 0.60 vs. 1.38 ±0.59 mmol/ liter in preterm, $P< 0.01$).[23]

MR Averna et al in their study suggested that dehydroepiandrosterone sulfate measurements in cord blood do not give any further information about transient neonatal hyper cholesterolemia.[24]

D J P Barker et al. in their study ‘Growth in utero and serum cholesterol concentrations in adult life’ found that, men and women who had a small abdominal circumference at birth had raised serum concentrations of low density lipoprotein, cholesterol and apolipoprotein B. This was independent of the duration of gestation. The association between abdominal circumference at birth and low density lipoprotein, cholesterol concentration was independent of social class, bodyweight, cigarette smoking, and alcohol consumption.[25]

Jagdish Singh et al. studied the cord Blood Cholesterol in Term and Pre term Newborns, (100 newborns, term and preterm were 78 and 22, respectively. Seventy seven babies weighed >2.5 kg and 23 were of <2.5 kg. Boys and girls were 56 and 44%, respectively). The mean cord blood cholesterol (±1 SD) level was 90.4 ±18.2 mg/dl with a range of 51.4-126 mg/dl. In term babies, the mean level was 96.2 ±15.1 mg/dl as compared to 69.5 ± 10.9 mg/dl in preterm ($p < 0.001$). The mean levels were 96.1 ± 15.0 and 66.8 ± 16.0 mg/dl in babies weighing >2.5 and <2.5 kg, respectively ($p < 0.001$). Serum cholesterol values showed significant positive correlation with gestational age and birth weight. [26]

Jones J N et al. studied the cord serum lipid levels associated with small for gestational age infants and found that, total cord serum lipid content was markedly decreased in all SGA infants compared with AGA infants (2.8 times lower).

Although SGA infants showed lower total lipid concentration, SGA I and SGA II infants showed distinct characteristics. Infants in the SGA I group had higher triglyceride levels (1.8 times higher) and lower free fatty acid levels (1.4 times lower), compared with AGA infants ($P < .001$). The lipid subclass distribution in SGA II infants was not significantly different from that in AGA infants, with the exception of an increase in triglyceride concentrations (1.3 times higher). Although the 22-kD placenta derived apolipoprotein A-I was similar in all groups, the level of fetal liver– derived 28-kD apolipoprotein A-I was 6.5 times lower in SGA I infants than in AGA or SGA II infants ($P < .001$).[9]

Molina M et al. in their study “Lipid profile in newborns with intrauterine growth retardation”, found that serum triglycerides levels were higher in newborns with intrauterine growth retardation, compared to (normal) term newborns.[10]

Claire L M et al. in their study ‘Long-term metabolic consequences of being born small for gestational age’ found that, reduced fetal growth is independently associated with an increased risk of the development of cardiovascular diseases, the insulin-resistance syndrome, or one of its components: hypertension, dyslipidemia, impaired glucose tolerance, or type 2 diabetes.

All of them appear to result from the initial development of insulin-resistance which appears as a key component underlying the metabolic complications. Although the mechanism remains unclear, there is some evidence that argues in favor of an active contribution of the adipose tissue in the emergence of insulin-resistance associated with in utero under nutrition.[27]

B Geloneze et al. in a study titled ‘Atherogenic lipid profile of Brazalian near term newborns’ in 2005 divided the cord blood of 135 newborns (66 males), into two groups: 25 near-term neonates (35-36 weeks of gestational age) and 110 term neonates (37-42 weeks of gestational age). The total cholesterol concentrations were higher in the near-term neonates than in the term group (94.04 ± 8.02 *vs.* 70.42 ± 1.63 mg/dl, $P < 0.01$), due to an increase in the LDL-cholesterol fraction in the

near-term group (57.76 ± 6.39 *vs.* 34.38 ± 1.29 mg/dl, P<0.001). The atherogenic indexes (total cholesterol/HDL-cholesterol, LDL cholesterol/HDL-cholesterol and apolipoprotein B/apolipoprotein A-I) were higher in the near term group (P < 0.001, P < 0.001, and P< 0.05, respectively).

The gestational age of the newborns was inversely correlated with total cholesterol and LDL-cholesterol, and also with the total cholesterol/HDL- cholesterol and LDL-cholesterol/ HDL-cholesterol indexes.[11]

Jane Oba et al conducted a study on 212 neonates out of them 107 was females and 105 were males. They found serum concentrations of total cholesterol, LDL and HDL cholesterol were higher in preterm then term newborns but triglyceride values were lower in preterm than term newborn. They also found that SGA newborns have higher levels of triglycerides, total cholesterol, HDL and LDL cholesterol compared to AGA.[28]

Hossain MA et al. measured the Serum triglyceride level in IUGR babies and they compared it with preterm AGA and term normal babies. Serum TG levels were estimated among three groups: IUGR (n=30), preterm appropriate for gestational age (AGA) (n=30) and term normal (n=30) new born babies. It was observed that serum TG level (54.4 ± 11.2 mg/dl) in IUGR babies were significantly higher than that of term normal babies (38.7 ± 5.8 mg/dl), p value < 0.05.[12]

Roya Kelishadia et al. showed that among 442 (218 boys and 224 girls) normal vaginal delivery newborns,14.4% were preterm and rest were full term, around 9.2% (n = 35) of the full-term newborns were small-for-gestational-age (SGA), of which 16 had a Ponderal index (PI) below the 10th percentile (SGA I) and 19 had above the 10th percentile (SGA II), 5.5% (n = 21) were large-for-gestational-age (LGA), and the remainder were appropriate-for-gestational-age (AGA).

Total and high-density lipoprotein cholesterol (HDL-C) in girls were significantly higher than in boys (80.3 ± 33.3 and 31.1 ± 9.9 vs. 73.3 ± 23.1 and 28.8 ± 8.7 mg/dL, respectively, $P < 0.05$). The mean apolipoprotein A (APO-A) of neonates with underweight mothers was significantly lower, and the mean APO-B level of those with overweight mothers was significantly higher than other neonates.

The mean low-density lipoprotein cholesterol (LDL-C), HDL-C and APO-A of the LGA newborns were significantly lower, and their APO-B was significantly higher compared to AGA and SGA neonates. The SGA I neonates had significantly lower total cholesterol, LDL-C, HDL-C and APO-A, as well as higher triglycerides, lipoprotein-A and APO-B than the SGA II group. The mean cord blood triglycerides of full-term neonates was significantly higher than preterm neonates (69.4 ±11.9 vs. 61.4 ± 12.7 mg/dl, respectively, $P = 0.04$).[29]

Cristina Catarino et al. studied the impact of maternal lipid changes upon the fetus in pre-eclampsia by evaluating lipid profile simultaneously in maternal and umbilical cord blood. Forty-two healthy pregnancies and

46 pregnancies complicated with pre-eclampsia were taken. Total cholesterol (TChol), HDL- cholesterol (HDLc), LDL-cholesterol (LDLc) and triglycerides (TG) levels were determined using enzymatic methods.

Apolipoprotein (APO) A I, APO-B and lipoprotein (a) [Lp(a)] values were measured by immunoturbidimetry. They found that Pre-eclamptic women presented significantly higher values for TChol, LDLc, HDLc, TG, APO-AI and APO-B compared to normal pregnant women. In the cord blood from pre-eclamptic pregnancies, significantly lower values for HDLc and APO A-I, and significantly higher TG concentrations and LDLc/HDLc ratio were observed when compared to normal cases. A positive correlation was observed between maternal TG levels and proteinuria, a marker of pre-eclampsia severity (r =0.40, p<0.01).

Their data suggested that pre-eclamptic pregnancy is associated with an enhanced hyperlipidemia, which seems to have a negative impact on fetal lipid profile, as reflected by a higher atherogenic LDLc/HDLc ratio and higher TG levels in cord blood. These children, born of women with PE, may deserve a closer clinical follow-up later in life.[30]

Badiee Z et al. cord lipid profile, apolipoprotein A, apolipoprotein B and lipoprotein a (LPa) were analysed in 378 full term newborns. Female neonates had significantly higher concentrations of TC and HDL-C than male neonates 81.4±28.3 Vs. 75.2±21.1, P=0.02 and 31.18±9.97 Vs. 28.8±8.7, P=0.0.02respectively. Other biochemical factors were not significantly different between gender.[31]

BIOCHEMISTRY OF LIPIDS

Lipids constitute a very important group of organic substances in animal tissues. The term LIPID was suggested by BLOOR and recommended by International union of Pure and Applied Chemistry. According to Bloor,[32] Lipids are compounds having the following characteristics:

1. Insolubility in water and solubility in one or more organic solvents (eg. Ether, Chloroform, Benzene, Acetone-the so called fat solvents)
2. Some relation to fatty acids and ether, either actual or potential.
3. Possibility of utilization by living organism

THE FOLLOWING CLASSIFICATION OF LIPIDS IS MODIFIED FROM BLOOR: [33,34]

SIMPLE LIPIDS

Esters of fatty acids with various alcohol.

a. FATS:Esters of fatty acids with glycerol. A fat in liquid state is known as oil.
b. b.WAXES: Esters of fatty acids with higher molecular weight monohydric alcohol.

COMPLEX LIPIDS

Esters of fatty acids with various alcohol and fatty acid.

a. PHOSPHOLIPIDS: Lipids containing, in addition to an alcohol, a phosphoric acid residue. They frequently have nitrogen containing bases and other substituents, eg. In glycerophospholipids the alcohol is glycerol and in sphingophospholipids, the alcohol is sphingosine.

b. GLYCOLIPIDS (GLYCOSPHINGOLIPIDS:Lipids containing a fatty acid, sphingosine and carbohydrate.

c. OTHER COMPLEX DISEASE: Lipids such as sulfolipids and amino lipids.

Lipoproteins may also be placed in this category.

Plasma lipids consist of **triacylglycerols** (16%), **phospholipids** (30%), **cholesterol** (14%), and **cholesteryl esters** (36%) and a much smaller fraction of unesterified long- chain fatty acids (free fatty acids) (4%). This latter fraction, the **free fatty acids (FFA),** is metabolically the most active of the plasma lipids.

PRECURSOR AND DERIVED LIPIDS: These include fatty acids, glycerol, steroids, alcohols in addition to glycerol and sterols, fatty aldehydes and ketone bodies, hydrocarbons, lipid soluble vitamins and hormones. Because they are uncharged acylglycerols (glycerides), cholesterol and cholestryl esters are termed neutral lipids.

FREE FATTYACIDS

Fatty acids are transported from their storage site in adipose tissue to their site of utilization as triglycerides and the rate limiting enzyme in this mobilization is a hormone sensitive lipase. Free fatty acids undergo oxidation re-esterification or conversion to other fatty acids. The major sites of oxidation are liver and heart in resting state and skeletal muscles during exercise. Fatty acids are taken up by liver are re-esterified to triglycerides and phospholipids. Normal mean plasma level is 12mg/100ml.

TRIGLYCERIDES

Triglycerides consists of glycerol esterified with three long chain fatty acids such as stearic (18 carbon atoms) and palmitic acid(16 carbon atoms).These together with fatty acids are saturated, certain unsaturated fatty acids are important as precursors of prostaglandins and in the esterification of cholesterol .Both saturated and unsaturated fatty acids are important components of cell membrane.

In general vegetable oils are triglycerides that are liquid at room temperature due to their higher unsaturated or shorter length carbon chain fatty acids. Triglycerides are the most abundant naturally occurring lipids. The type formula of fat or oil is as follows: Usually R1 and R2 are saturated fatty acids and R2 is unsaturated fatty acid. Since all three of the glycerol alcohol groups are esterified, these fats are termed as triglycerides.

The chief source of dietary fats is obtained endogenously from liver and small intestine. Dietary triglycerides have relatively short half life in plasma and are removed mostly by adipose tissue, thus the measurements of fasting sample reflects the amounts of endogenous triglycerides.

CHOLESTEROL: [34,35]

It is a sterol possessing a four ringed steroid nucleus and a hydroxyl group. It occurs in both free and esterified forms. Free cholesterol is a component of all cell membranes. The esterified form predominates in adrenal cortex, plasma and athermanous plaques. Under normal circumstances, virtually all the newly synthesized cholesterol originates from the liver and distal part of small intestine. Fecal excretion in the form of natural esterol and bile acids about 1gm/day, balances the synthesis and absorption. In childhood, normal values vary from 42-205mg/dl.

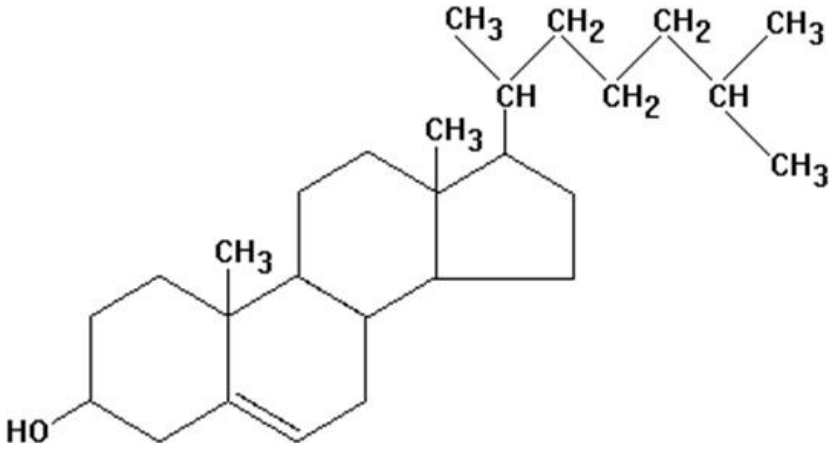


FIGURE 1: STRUCTURE OF CHOLESTEROL[34]

LIPOPROTEINS: [34,35]

Lipoproteins are proteins conjugated to a lipid like lecithin, cephalin, and neutral fat. These are globular particles of very high molecular weight that transport non polar lipids (triglycerides and cholesterol) in the circulation to liver and peripheral tissues.

Since lipids are insoluble in water, the problem of how to transport them in the aqueous blood plasma is solved by associating nonpolar lipids (triacylglycerol and cholesteryl esters) with amphipathic lipids (phospholipids and cholesterol) and proteins to make water miscible lipoproteins.

In addition to FFA, four major groups of lipoproteins have been identified that are important physiologically and in clinical diagnosis. These are

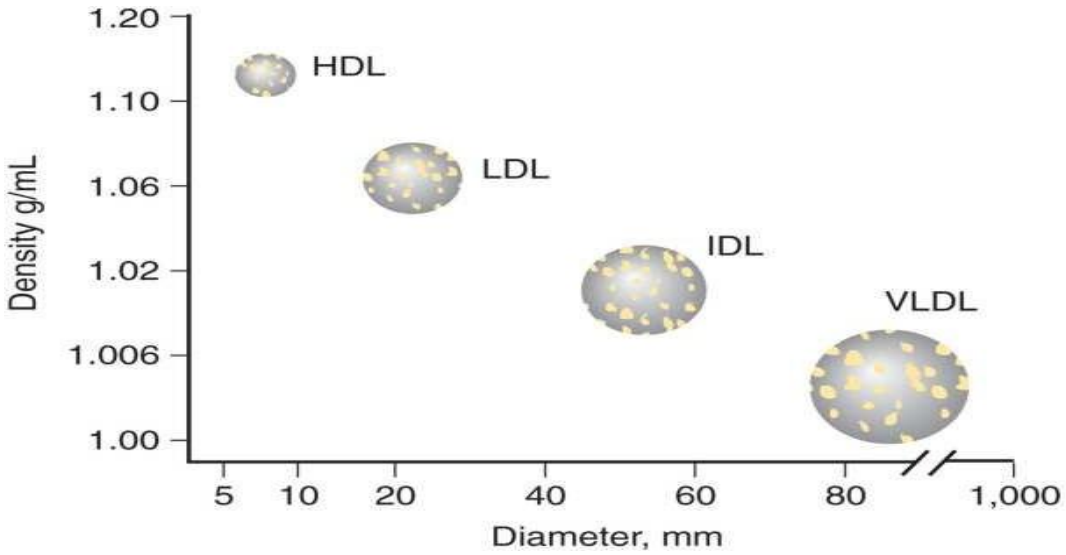
a) **Chylomicrons** derived from intestinal absorption of triacylglycerol and other lipids;

b) **Very Low Density lipoproteins** (VLDL, or pre-β-lipoproteins), derived from the liver for the export of triacylglycerol;

c) **Low-Density lipoproteins** (LDL, or β- lipoproteins), representing a final stage in the catabolism of VLDL; and

d) **High-Density lipoproteins** (HDL, or α-lipoproteins), involved in VLDL and chylomicron metabolism and also in cholesterol transport.

FIGURE 2: THE DENSITY OF THE SEVERAL CLASSES OF LIPOPROTEIN IS INVERSELY PROPORTIONAL TO THE RATIO OF LIPID TO PROTEIN



Lipoproteins function both to keep their component lipids soluble as they transport them in the plasma, and also to provide an efficient mechanism for transporting their lipid contents to (and from) the tissues.

Lipoproteins mediate this cycle by transporting lipids from the intestines as chylomicrons and from the liver as very low density lipoproteins (VLDL) to most tissues for oxidation and to adipose tissue for storage.

Triacylglycerol is the predominant lipid in chylomicrons and VLDL, whereas cholesterol and phospholipids are the predominant lipids in LDL and HDL, respectively Lipoproteins may be separated according

to their electrophoretic properties into α**,** β**,** and pre β-lipoproteins.

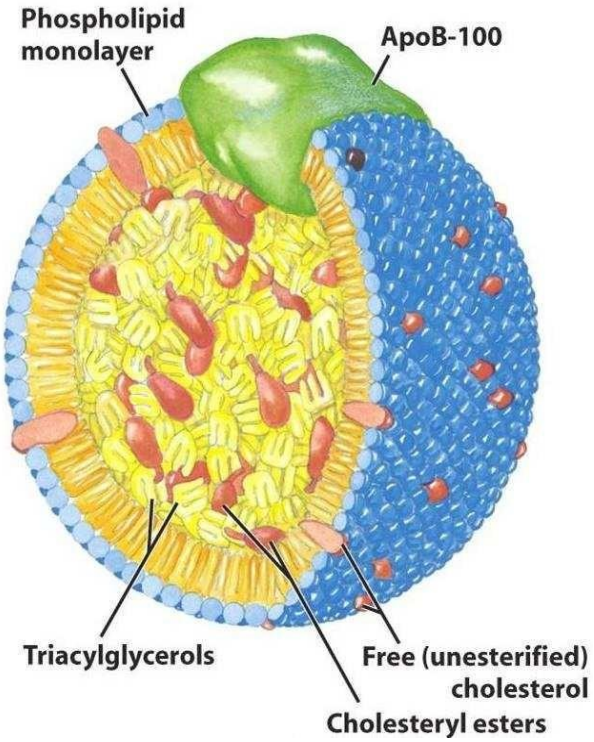
The constituents of these macro molecular complexes includes triglycerides, cholesterol, phospholipids and apolipoproteins. Each complex particle contains a nonpolar core mostly triglycerides and cholesterol in varying proportions with a polar surface coat of phospholipids, so that it can remain in solution in plasma. Plasma lipoproteins differ according to the flotation rate, hydrated density, size and electrophoretic mobility.

STRUCTURE OF A PLASMA LIPOPROTEIN:[34,35]

The nonpolar lipid core consists of mainly triacylglycerol and cholesteryl ester and is surrounded by a single surface layer of amphipathic phospholipid and cholesterol molecules. These are oriented so that their polar groups face outward to the aqueous medium, as in the cell membrane. The protein moiety of a lipoprotein is known as an apolipoprotein or apoprotein, constituting nearly 70% of some HDL and as little as 1% of chylomicrons.

The plasma lipoproteins are spherical macromolecular complexes of lipids and specific proteins (apolipoproteins or apoproteins). They differ in lipid and protein composition, size, and density.

FIGURE 3: STRUCTURE OF A PLASMA LIPOPROTEIN[35]



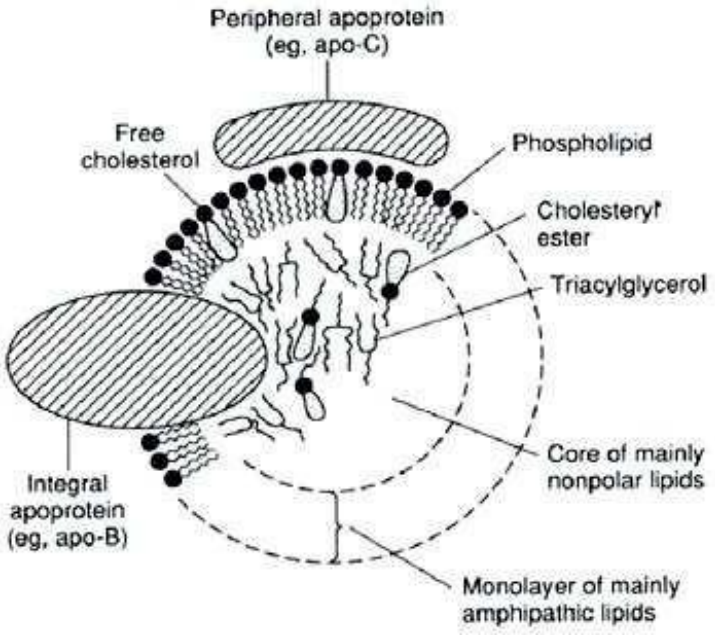


Figure 4: Structure of a Plasma Lipoprotein

Apoproteins are the protein moiety of lipoproteins.[34,35]

They have three main functions:-

1) They regulate the reactions of these lipids with enzymes.

2) They help solubililize cholesterol esters and triglycerides.

3) They bind to cell surface receptors and thus determine the sites of uptake and rates of degradation of other constituents especially cholesterol.

Are also Constituent proteins. They are responsible for a variety of metabolic functions in addition to their structural role, including cofactors or inhibitors of enzymatic pathways, and mediators of lipoprotein binding to cell surface receptors. ApoA is the major apoliprotein of HDL. ApoB is present in LDL, VLDL, IDL, and chylomicrons. ApoB-100 is derived from the liver, whereas apoB-48 comes from the small intestine. ApoC-I, C-II, and C-III are small peptides important in triglyceride metabolism. Likewise, apoE, which is present in VLDL, HDL, chylomicrons, and chylomicron remnants, plays an important role in the clearance of triglycerides.

High levels of VLDL and LDL in serum indicate that the individual is at risk with regard to protective effect against the development of atherosclerosis. Normal plasma LDL and VLDL levels in childhood vary in childhood varies from 63-136 mg/dl.

High levels of VLDL and LDL in serum indicate that the individual is at risk with regard to protective effect against the development of atherosclerosis. Normal plasma LDL and VLDL levels in childhood varies from 63-136mg/dl and 4-24mg/dl respectively.

LIPID AND SEX VARIATION:[36,37]

No statistically significant difference in the levels of lipids was found in boys and girls in the same age group till puberty. HDL levels decline in both during puberty. In girls the HDL level subsequently increases to the pre pubertal concentration. In boys the level remains low after puberty. Males have higher LDL cholesterol but low HDL cholesterol than females .The lower incidence of coronary heart disease in women could be related to their persistently higher HDL concentration than males or lower LDL levels. This finally establishes the different lipoprotein patterns seen in adults.

FAMILIAL INFLUENCES AND AGGREGATION

The incidence of coronary artery diseases reached epidemic proportion in most developed countries and is gradually rising in developing countries.[39] Of all coronary risk factors the importance of hyperlipoprotenemia and hyperlipidaemia looms large. At least 3 lipoprotein disorders of familial type viz, type 2, 3 and 4 are known to accelerate atherosclerotic changes and hence premature coronary artery disease.[40] Except for type 2 hypertriglyceridemia where inheritance pattern is by a single gene defect, most of other triglyceridemia show

multi-factorial inheritance. A study by Krishna Kumar et al.[41] on "Serum Lipid Profile in children of parents with coronary artery diseases" showed that Coronary Artery disease is a striking at more and more younger subjects. Hyperlipidaemia and hyperlipoproteinemia are associated with premature atherosclerosis and children of coronary artery diseases patients are at greater risk to develop coronary artery diseases as these lipid abnormalities are genetically transmitted.

Neonatal familial type 2 hyperlipoprotenemia may often be identified by elevated levels of cord blood cholesterol and LDL cholesterol.[42] A study by J. Dogra et al.[43] on the serum lipids in neonatal cord blood in families with diabetes mellitus type-1 suggests the role of genetic factors in transmission of hypercholesterolemia in families affected with diabetes mellitus type-1.Thus a periodic surveillance of neonates belonging to these families can benefit in an earlier detection of atherosclerosis.

R.C.Tsang et al.[44] in their study of cholesterol at birth and at the age of one year recommended that hypercholesterolemia can be diagnosed by estimation of cord blood cholesterol and LDL cholesterol.

A study by T.J.C Boultan[33] comparing the relative influence on the children total cholesterol of nutritional and a family history of early coronary heart diseases were found to be important correlates of the children's total cholesterol level become increasing important from the end of the 1st year ,or that the effect of these influences is obscured

during infancy by other ,presumably nutritional factors, which themselves are elusive because of the inherently inadequate methodological techniques of dietary studies.

CORD BLOOD LIPID PROFILE AND NEONATES:[42]

Neonatal familial type-2 hyperlipoprotenemia may often be identified by elevated levels of cord blood cholestrol and LDL cholesterol.

A study by Reginald Tsang et al on cord blood hypertriglyceridemia, was originally designed to assess the utility of cord blood cholesterol analysis in the diagnosis of neonatal and familial type-2 hyperlipoprotenemia. The data suggested that hypertriglyceridemia at birth is an indicator or ante partum fetal stress or compromise. It is possible that quantization of cord blood triglyceride might provide a rapid, easily available, and in expensive measure that could be used prospectively or retrospectively in analysis of ante partum or intra partum factors that adversely affect the fetus.

SERUM LIPIDS AND DIET:[43,44,45,46]

In a study by T.J.C.Boultan,[33] serum cholesterol in early childhood, comparing the relative influence on the children's total cholesterol of nutritional and familial factors, the parent's total cholesterol and family history of early coronary heart disease were found to be important correlates of the children's total cholesterol. Low correlations occurred

for nutritional factors. While comparing the breast fed and formula fed infants, a number of workers have found significant effects directly depending upon polyunsaturated fatty acids and cholesterol content of the formula.

Familial hypercholesterolemics on moderate to high cholesterol intake at one year maintain distinctive elevation while low cholesterol diet reduces the differences between index and controls.

There is much inter individual variations in response to dietary fats**.** The great differences in the plasma cholesterol in various countries are also related to difference in dietary habits. The saturated fatty acids definitely raise the total cholesterol levels while polyunsaturated fatty acids have cholesterol lowering action. Monounsaturated fatty acids have no effect i.e. are neutral. Dietary cholesterol increases the serum cholesterol levels possibly by suppressing the hepatic LDL receptors.

Carbohydrates and fibers also affect the metabolism of lipoproteins. Increased intake stimulates the hepatic synthesis of triglycerides and can increase LDL levels and decrease HDL cholesterol levels.

LIPID PROFILE AND TERM NEONATES:

Several studies have revealed that the concentration of total cholesterol, VLDL+LDL cholesterol and triglyceride are low compared to adults and have wide range. Nearly 50% of total cholesterol and 30%

of total triglyceride is present in HDL constitutes a higher percentage of total lipoproteins as compared to adults.[45]

LIPID PROFILE AND PRETERM AND LOW BIRTH WEIGHT BABIES:

The preterm and low birth weight new born have higher cord blood triglycerides as compared to normal full term newborns according to a study on serum lipid status in neonates by N.Haridas, P.T.Acharya.[45] In low birth weight infants this could be indicative of intrauterine malnutrition and starvation. But no difference was found in respect of cholesterol level in the cord blood. The vast difference between cord blood and maternal lipids reveal the possible lack of maternal contribution of fetal lipids.

The Low Birth Weight Infants are born with intrauterine malnutrition. Such circumstances favour fetal adipose tissue breakdown liberating free fatty acids .That portion of free fatty acids that escapes oxidation for energy is synthesized in liver into triglycerides which cause elevated levels of triglycerides in low birth weight as compared to normal full term infants. Intrauterine malnutrition resembling marasmus and starvation in other children could be the result of placental insufficiency. The normal full term ones on the contrary are in receipt of a ready placental supply of nutrients, and so there is very little need for lipolysis in utero.[26] While contrary findings were reported by P.K.Mishra et al.[46]

Higher free fatty acids and triglyceride levels in the cord blood of SGA neonates may be due to release of free fatty acids from fat stores for energy metabolism in presence of intrauterine malnutrition. In the intermediate postnatal period lower level of free fatty acids in these newborn compared to control may be result of relative depletion of fat stores by the intrauterine release. The high levels of triglycerides in the fasting state may be as a result of very high triglyceride levels in the cord blood. The lesser rise in the free fatty acids levels in preterm AGA of 28-32weeks gestation may be as a result of insufficient lipid stores and lipolysis in them.[46]

LIPIDS AND ATHEROSCLEROSIS:

The clinical interest in serum lipids, lipoproteins and apolipoproteins is related almost exclusively to their relationship to atherosclerosis. In recent times considerable epidemiological evidence has accumulated in support of a strong association between raised cholesterol concentration and subsequent risk to the development of the coronary artery disease. Furthermore number of investigators**,** now considers only LDL and high density lipoproteins worthy of consideration as major risk factors in the development and progression of atherosclerotic vascular disease.[47,48]

The American Heart Association and National Heart, Lung and Blood Institute in a joint statement has presented overwhelming evidence to support the continuous and positive correlation of coronary artery

disease with blood cholesterol level .One percent reduction in an individual total cholesterol translates into approximately two percent reduction in coronary artery risk.

Low serum cholesterol levels are accompanied by prolongation of life and improvement in the quality of life and is ever beneficial for people who already had coronary heart disease.[49]

George Steiner bet al.[49] in their study of "The association of increased levels of intermediate density lipoproteins with smoking and with coronary artery disease" showed that HDL cholesterol was somewhat reduced in those with coronary artery disease. The possible importance of HDL lies in the demonstration of a "protective" effect of this lipoprotein in relation to coronary artery disease and the frequent, but not invariable, inverse relationship between HDL and plasma triglyceride levels. Because of its importance in triglyceride transport, they paid particular attention to the levels of intermediate density lipoproteins. The association of LDL with documented coronary artery disease may be important in consideration of the relationship of hypertriglyceridemia to atherosclerosis, particularly in view of large proportion of triglyceride-rich lipoproteins found in LDL.

Increased concentration of LDL have been reported in patients with renal failure, type -3 hyperlipoproteinemia and possibly diabetes, and may contribute to the accelerated atherosclerosis observed in these patients. Their study pointed out the association of LDL with atherosclerosis.

The protective role of HDL cholesterol has been well established by a number of workers. Elevated HDL cholesterol is antiatherogenic and a low level is an independent risk factor for coronary artery disease. Since HDL cholesterol participates in reverse transport of cholesterol it reduces the accumulation of cholesterol in arterial wall or prevents the formation of thrombi on atheromatous plaques by stabilization of prostacyclines.

THE CHILD AND ATHEROSCLEROSIS:

Connar S L et al.[37] in their study found that the mean cholesterol concentration in males were higher in childhood and lower at post puberty. Thereafter, it generally increased with age, attaining a maximum mean concentration at age 55-60 years. The mean plasma LDL cholesterol concentrations paralleled the age related increase in the total plasma cholesterol. A general drop in the HDL cholesterol levels occurred through childhood and early adulthood, followed by an increase with age in females and no increase in males.

In children, the correlation coefficients were strikingly different from those in adults. The total cholesterol, LDL and HDL did not correlate with age or adiposity. As in adults, however the plasma triglyceride correlated with age, weight and adiposity. Plasma cholesterol, LDL cholesterol and triglyceride, remained positively correlated with age after adjusting for weight. Similarly the plasma triglyceride remained correlated with weight after adjusting for age.

The fatty streaks appear in coronary arteries at about the age of 15 years and these were found to be significantly related to levels of total cholesterol, VLDL cholesterol and systolic blood pressure. The fate of fatty streaks is not well established but animal studies suggest that they may remain unchanged, disappear or ultimately develop into athermanous plaque. The presence of fatty streaks in arteries of new born and children implies that preventive measures should be instituted early in life, before these streaks transforms into adult atheromas. Early prevention becomes more important in childhood as good dietary habits are also formed during this period which has a bearing upon serum lipids.[50,51,52]

LIPID PROFILE AND SGA NEONATES:

Levels of lipids and lipoproteins in cord sera should be a reflection of the status of plasma lipid metabolism in the infant at birth. Most fetal lipids are synthesized de novo through the conversion of glucose to various fatty acids- containing compounds. Where as part of lipids are obtained from the maternal circulation by the placenta principally in form free fatty acids and cholesterol, and this transfer increases as the gestational age advances, and this deposition is more in the last trimester.[53]

It is known that premature newborns including SGA babies have lost the chance to complete their energy deposits because of preterm delivery. Thus, many times the preterm neonate needs to use these endogenous reserves, basically activating lipid metabolism that generates energy and promotes gluconeogenesis, where by altering lipid metabolism in this high risk babies.[54]

The lipid profile of the SGA group indicated markedly diminished fetal liver– derived apolipoprotein A-I levels and decreased absolute total lipid levels; however, at relative concentrations, triglycerides were elevated and free fatty acids lowered. Those alterations are consistent with an inability to hydrolyze circulating triglycerides, because of decreased activity of lipoprotein lipase enzyme, leading to diminished peripheral adipose deposition. The lower free fatty acid levels in the absence of adequate peripheral adipose deposition might be consistent with depletion, secondary to use as an alternate fuel source or might be simply a reflection of a more severe degree of uteroplacental insufficiency in that group.[55]

The underlying mechanism linking SGA with adverse lipid levels is not well understood. It is generally assumed that factors influencing insulin sensitivity may explain the association between birth weight and dyslipidemia.[56]

Hyperinsulinemia is known to enhance hepatic very-low-density lipoprotein synthesis, which may contribute to increased plasma triglycerides and LDL-c levels. Resistance to the action of insulin on lipoprotein lipase in peripheral tissues may also contribute to elevated triglyceride and LDL-c levels.[56]

Other mechanism includes decrease in the activity of the lectin acetyl cholesterol transferase (L CAT) enzyme; the fall in HDL-cholesterol levels may be associated with a decrease in the activity of the lectin acetyl cholesterol transferase enzyme. Studies have demonstrated that lectin acetyl cholesterol transferase activity is lower in near term neonates (SGA) compared with the term infants.[56]

Even the concentrations of apolipoprotein A-I and apolipoprotein B were significantly different in near term babies (SGA), many studies have shown that a trend towards a worse lipid profile in the near-term group (SGA), with higher apolipoprotein B levels, related to low-density lipoproteins, and lower apolipoprotein A-I levels, related to the inverse cholesterol transport, that protect against atherosclerotic lesions. Moreover the apolipoprotein B/apolipoprotein AI index, considered to be one of the best markers of risk for cardiovascular disease even during the first year of life, was significantly higher in the near-term neonate group compared with the term group, demonstrating that this index is altered even in umbilical cord blood…

Many studies have demonstrated that total cholesterol, LDL-cholesterol fraction and atherogenic indexes are significantly higher in near term neonates compared with term infants, showing a trend to a worse lipid profile in near-term infants. Future studies are needed to determine if this atherogenic profile in near-term neonates can affect body metabolism, increasing the risk for cardiovascular diseases in adult life.

FETAL LIPOGENESIS:[34]

The three principle pathways of fatty acid synthesis are:

1. De novo synthesis in the cytosol of the cell.

2. Fattyacids chain elongation by microsomes.

3. Fattyacids chain elongation by mitochondria.

De novo synthesis of long chain fatty acids from acetyl coenzyme A (COA) is the primary synthetic pathway in most cells.

The net reaction involved in denovo synthesis of fatty acids, using palmityl COA as an example, is

8Acetyl-COA+14NADPH+14H□+FATP+H2O□Palmitic acid+8COA+14NADP+FADP+FPI

De novo synthesis of fatty acids requires a series of enzyme controlled reactions. The initial reaction of de novo synthesis, the carboxylation of acetyl COA to form malonyl COA, is catalyzed by the enzyme acetyl COA carboxylase. This enzyme is thought to be the rate limiting enzyme for fatty acids synthesis. In the subsequent series of reactions, the fatty acids synthetase complex catalyses the synthesis of 1 mole of palmitic acid from 7 moles of malonyl COA and 1mole of acetyl COA,ATP and NADPH provide the energy required for this complex series of reaction.

Long chain fatty acids are synthesized by the chain elongation of preexisting fatty acids. In mitochondria, the reversal of □-oxidation with the resulting incorporation of acetyl COA into pre existing fatty acids results in fatty acids chain elongation by the sequential addition of two carbon subunits. The microsomal and mitochondrial elongation pathways play a relatively minor role in fatty acids synthesis compared to de novo synthesis .One possible exception is in the heart where mitochondrial chain elongation is the only pathway for long chain fatty acids synthesis.

PRECURSORS OF FETAL LIPOGENESIS:[34,35]

Carbohydrates in the form of glycogen, glucose and lactate have been reported to be the major precursors for de novo synthesis of fatty acids in the fetus and neonate. Nearly 40%of all maternal glucose that is perfused into the placenta is metabolized to lactate by the placenta. One possible reason for the preferences of the lactate to glucose as a precursor for lipogenesis is that lactate exists in a high redox state.

Conversion of lactate to pyruvate results in the conversion of NAD to NADH. Lactate may indirectly provide the NADPH required for de novo synthesis of fatty acids. Determination of the presence of transhydrogenases in these fetal tissues in which de novo synthesis of fatty acids occurs (eg.Lung, Liver and adipocytes) would support this theory.

Glucose, amino acids and ketone bodies have been investigated as precursors for lipid synthesis. Amino acid was found to be a minor precursor for fetal adipose tissue lipogenesis.

To determine if substrate availability of glucose controls fetal lipogenesis in vivo Ktorza et al induced mild hyperglycemia in unrestrained pregnant rats at 20.5-23.5 days of pregnancy by infusing glucose. They reported that total carcass fat of the fetus is increased over control levels and that the rate of lipogenesis is significantly greater in the hyperglycemic fetuses, suggesting that substrate availability of glucose does control fetal lipogenesis.

THE BARKER HYPOTHESIS:

David Barker M.D.[64] Ph.D. FRS is a Physician and Professor of Clinical Epidemiology at the University of Southampton, UK and Professor in the Department of Cardiovascular Medicine at the Oregon Health and Science University, US. Twenty years ago, he showed for the first time that people who had low birth weight are at greater risk of developing coronary heart disease. In 1995, the British Medical Journal named this the “Barker Hypothesis.” and is now widely accepted. [64]

The observation that deaths from ischemic heart disease appeared linked to birthplace led to the suggestion that pre-natal and early post-natal factors may be risk factors for ischemic heart disease. This hypothesis was first formally tested by Barker et al.[64,65] who examined the mortality records of 5654 men born during 1911– 1930 in

Hertfordshire, England. This study showed that men with the lowest weights at birth subsequently had the highest death rates from ischemic heart disease. This association between coronary heart disease and small size at birth has now been replicated in a number of studies in Europe,[66,67] North America[68] and India.[69]

As a consequence of these findings, Barker[64,70] proposed the concept of a 'fetal origin of coronary heart disease'. In essence this model proposes that in response to under nourishment; the fetus undergoes a number of physiological and metabolic adaptations. These adaptations persist post-natally and predispose the individual to coronary heart disease in later life. Since the original formulation of this hypothesis, further work has led to a number of refinements in this theory.

There is now growing awareness that the long-term effects of intrauterine under nutrition depend upon its timing during gestation. Retrospective analyses of babies born during the Dutch famine of 1945 have shown an association between CHD and early (as opposed to late) nutritional challenges during gestation.[71]

Similarly, there is increasing evidence of the importance of not only the pre-natal environment, but also the early post-natal environment as a determinant of cardiac disease. Eriksson et al.[72] have recently shown an association between CHD and rapid childhood weight gain, and this finding has now been replicated in other studies. Napoli et al.[73] Have shown that maternal hypercholesterolemia during pregnancy induces changes in the fetal aorta that determine the long- term susceptibility of children to subsequent atherosclerosis.

Dr. Barker's work is relevant to both Western countries and the Third World. In the Western world, many babies remain poorly nourished because their mothers eat diets that are unbalanced in macronutrients and deficient in micronutrients, or because their mothers are excessively thin or overweight. In the Third World, many girls and young women are chronically malnourished.

Coronary heart disease (CHD), hypertension, and diabetes mellitus (DM) occur in epidemic proportions worldwide. Unhealthy lifestyle practices and behaviors are well accepted as contributing factors, but the true origins of these diseases may actually be found in utero.

Finally, according to the Barker hypothesis, disturbed intrauterine growth has a negative influence on the development of the cardiovascular system and favors the occurrence of hypertension, insulin resistance, Diabetes mellitus, hypercholesterolemia, and hyperuricemia in adult life.[64]

MATERIALS AND METHODS

STUDY DESIGN: This is a Cross – sectional Hospital based study.

SOURCE OF DATA:

This study was conducted at GOVT KILPAUK MEDICAL COLLEGE HOSPITAL during the term between MARCH 2018 TO AUGUST 2018.

Study subjects included 100 babies in which 50 babies had birth weight above 2.5 kg and 50 babies had birth weight below 2.5 kg..

INCLUSION CRITERIA:

Term babies with birth weight more than 2.5 kg

(GROUP A)

Preterm babies with birth weight less than 2.5kg

(GROUP B)

EXCLUSION CRITERIA:

1) Neonates with any Congenital malformations.
2) Neonates born to mother with maternal illness like Diabetes mellitus (DM) including Insulin dependent diabetes mellitus (IDDM) & gestational diabetes, Tuberculosis, Asthma, Pregnancy induced hypertension, thyroid disease.
3) Neonates with family history of coronary heart disease / hypercholesterolemia.
4) Any maternal medication, except iron & vitamin supplements.
5) Drug abuse in mother and antenatal medications
6) Instrumental delivery including extraction
7) Neonates with one minute Apgar score <7 at 5min

METHOD OF THE STUDY:

This hospital based prospective study was carried out at NICU unit at GOVT KILPAUK MEDICAL COLLEGE CHENNAI 10 from MARCH 2018 to AUGUST 2018. Newborn babies delivered during this period who fulfilled the inclusion criteria were enrolled in this study.

All the subjects were included after obtaining written informed consent from parents/ guardian.

5 ml of cord blood was collected from the umbilical cord immediately after the delivery from the placental end of the cord just after the delivery of the baby in a plain dry test tube. Cord blood was allowed to clot and then immediately sent to lab where the samples were centrifuged at 400×for 10 minutes, and then serum was separated and stored at -20 ^{0}C until analysis.

After the delivery, the babies were examined, weight was recorded on electronic weighing scale, length was recorded with the help of infantometer, head circumference, chest circumference and other relevant anthropometric data were recorded using non stretchable measuring tape. Gestational age was calculated from the first day of the last menstrual period and confirmed by clinical assessment using modified New Ballard's score.

A thorough clinical examination of the newborn was done and weight of the baby was calculated by electronic weighing scale. Classification of infants was done based on gestational age as term and preterm newborn based on New Ballard's scoring.

Babies were classified as AGA and SGA with the help of intrauterine growth charts. Intrauterine growth charts developed at AIIMS were used to assess the weight for gestational age.

Lipid profile was done by using Auto analyser (Erba Mannheim, Transasia bio-medical LTD). TC estimated by using Modified Roeschlau method, TG estimated by using Wako and the modification by McGowan et al. and Fossati et al. HDL and LDL estimated based on a modified polyvinyl sulfonic acid (PSV) and polyethylene- glycol methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PSV/PEGME and selected detergents. VLDL estimated by TC/5 and Atherogenic index (AI) by TC/HDL.

STATISTICAL ANALYSIS

Results were expressed as mean ± standard deviation for continuous variables and as number and proportion (%) for categorical data. Since all data are known to be normally distributed, the parametric tests were used for statistical analyses. Differences between normal birth weight and low birth weight and SGA, AGA neonates as well as between male and female neonates were determined by Student's t test.

Chi square test was applied to test the association between two categorical factors. All the tests of significance were applied at 5% level of significance.

Statistical software: The package EPI-INFO version 3.5.3 was used for the analysis of the data and Microsoft Excel was used for data entry as well as to generate graphs, tables etc.

STATISTICAL METHODS

Lipid profile parameters were considered as primary outcome variables. Birth weight category(normal birth weight Vs low birth weight), Gender, AGA Vs SGA was considered as primary explanatory variable.

All Lipid profile parameters like triglycerides, total cholesterol, VLDL cholesterol, LDL cholesterol, HDL cholesterol were checked for normal distribution within each category of birth weight category by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

For normally distributed Lipid profile parameters the mean values were compared between study groups using Independent sample t-test (2 groups) P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(1)

1. IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

OBSERVATION AND RESULTS

A total of 100 subjects were included in the final analysis.

Table 1

Descriptive analysis of birth weight category in the study population (N=100)

Birth weight category	Frequency	Percentages
Normal birth weight	50	50.00%
Low birth weight	50	50.00%

Figure 5

Pie chart of birth weight category in the study population (N=100)

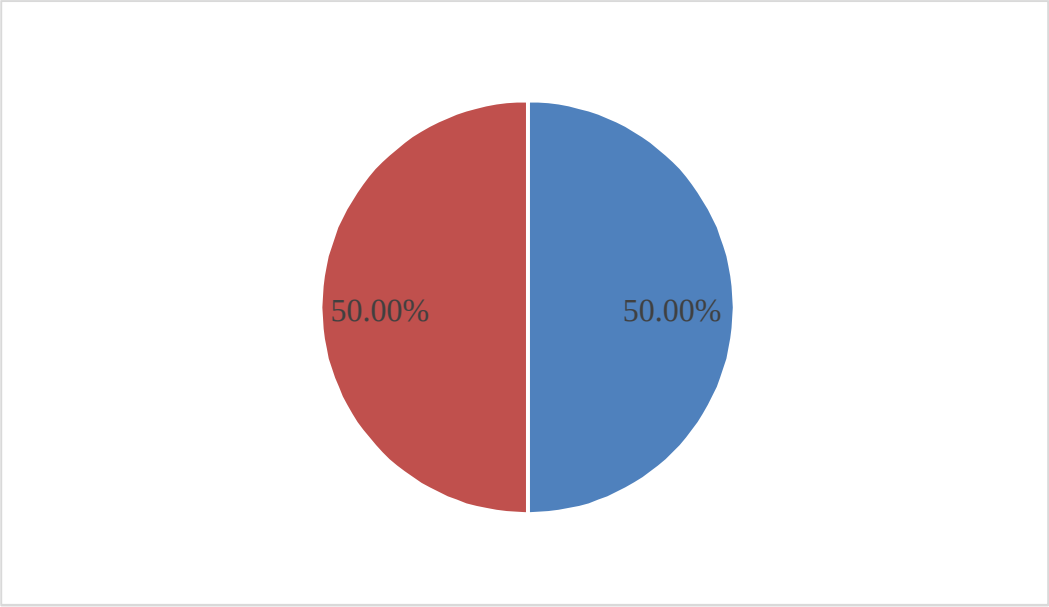


Table 2

Descriptive analysis of lipid profile in the study population (N=100)

Parameter	Mean ± SD	Median	Min	Max	95% C.I	
					Lower	Upper
Triglycerides (mg/dl)	52.81± 11.73	52.00	32.00	76.00	50.48	55.14
Total Cholesterol (mg/dl)	94.64 ± 10.89	95.00	70.00	107.00	92.48	96.80
VLDL Cholesterol (mg/dl)	10.29 ± 2.87	10.00	5.00	16.00	9.72	10.86
LDL Cholesterol (mg/dl)	66.24 ± 5.06	66.50	52.00	76.00	65.24	67.24
HDL Cholesterol (mg/dl)	23.94 ± 2.41	24.00	19.00	29.00	23.46	24.42

The mean total cholesterol was 94.64 ± 10.89in the study population, range between 70 mg/dl to 107 mg/dl in the study population (95% CI 92.48 to 96.80). The mean triglyceride was 52.81 ± 11.73in the study population, range between 32 mg/dl to 76 mg/dl in the study population (95% CI 50.48to 553.14). The mean HDLcholesterol was 23.94 ± 2.41in the study population, range between 19 mg/dl to 29 mg/dl in the study population (95% CI 23.46 to 24.42). The mean LDLcholesterol was 66.24 ± 5.06in the study population, range between 52 mg/dl to 76 mg/dl in the study population (95% CI 65.24 to 67.24). The mean VLDLcholesterol was 10.29 ± 2.87in the study population, range between 5 mg/dl to 16 mg/dl in the study population (95% CI 9.72 to 10.86). (Table 2)

Table 3

Comparison of mean of lipid profile parameters between Birth weight category (N=100)

lipid profile Parameter	Birth weight category		P value
	Normal birth weight (N=50)	Low birth weight (N=50)	
Total Cholesterol (mg/dl)	93.94 ± 4.35	95.34 ± 14.82	*0.523*
Triglycerides (mg/dl)	42.72 ± 5.38	62.9 ± 6.43	*<0.001*
HDL Cholesterol (mg/dl)	23.44 ± 2.56	24.44 ± 2.16	*0.037*
LDL Cholesterol (mg/dl)	64.86 ± 4.29	67.62 ± 5.42	*0.006*
VLDL Cholesterol (mg/dl)	7.88 ± 1.3	12.7 ± 1.75	*<0.001*

The mean Triglycerides of normal birth weight group was 42.72 ± 5.38(mg/dl)and low birth weightgroup was 62.9 ± 6.43(mg/dl), and the mean difference between two groups was statistically significant (P value<0.001). The mean Total Cholesterol of normal birth weight group was 93.94 ± 4.35(mg/dl)and low birth weightgroup was 95.34 ± 14.82(mg/dl), and the mean difference between two groups was statistically not significant (P value 0.523). The mean HDL Cholesterol of normal birth weight group was 23.44 ± 2.56 (mg/dl)and low birth weightgroup was 24.44 ± 2.16(mg/dl), and the mean difference between two groups was not statistically significant (P value 0.037). The mean

LDL Cholesterol of normal birth weight group was 64.86 ± 4.29 (mg/dl)and low birth weightgroup was 67.62 ± 5.42 (mg/dl), and the mean difference between two groups was not statistically significant (P value 0.006). The mean VLDL Cholesterol of normal birth weight group was 7.88 ± 1.3 (mg/dl)and low birth weightgroup was 12.7 ± 1.75 (mg/dl), and the mean difference between two groups was statistically significant (P value<0.001). (Table 3 & Figure 2 to 6)

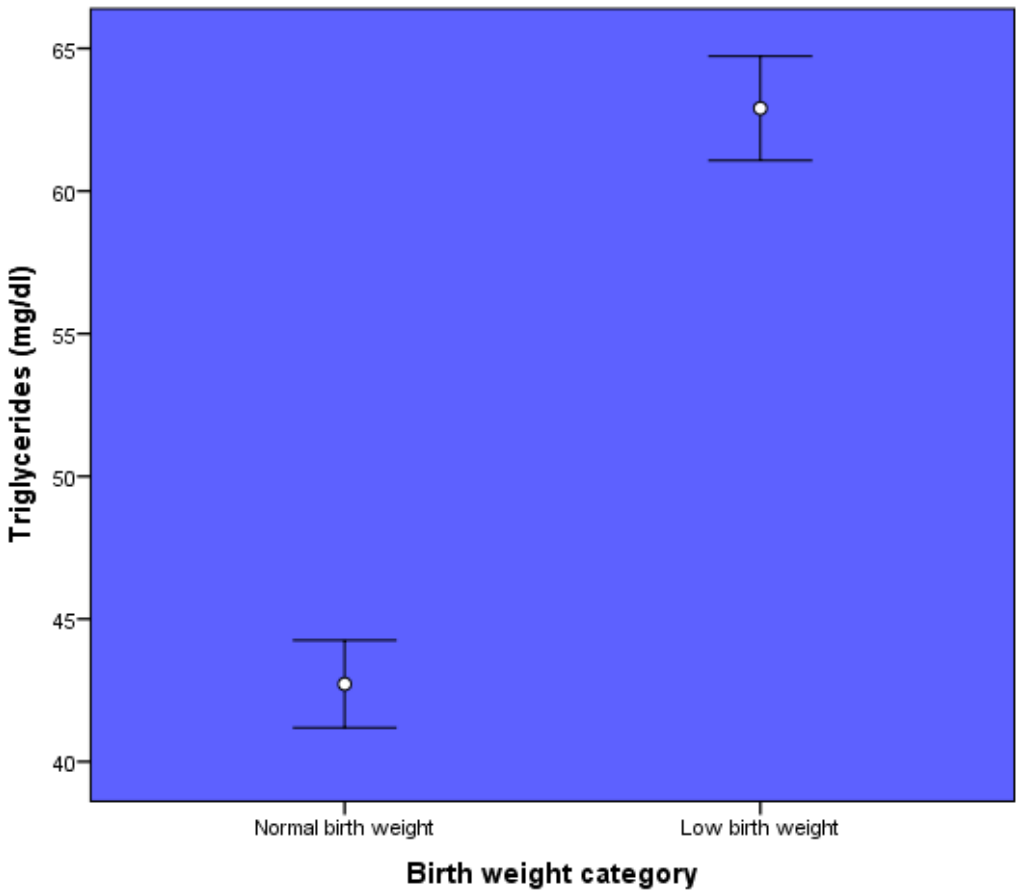
Table 4

Comparison of mean triglycerides (mg/dl) between birth weight category(N=100)

Birth weight category	Triglycerides (mg/dl) Mean± SD	Mean difference	95% CI		P value
			Lower	Upper	
Normal birth weight	42.72 ± 5.38	20.18	17.83	22.53	*<0.001*
Low birth weight	62.9 ± 6.43				

Figure 6

Error bar diagram of Comparison of mean triglycerides (mg/dl) between birth weight category (N=100)



This Diagram shows significant difference in Triglycerides level in between Normal and Low birth weight babies.

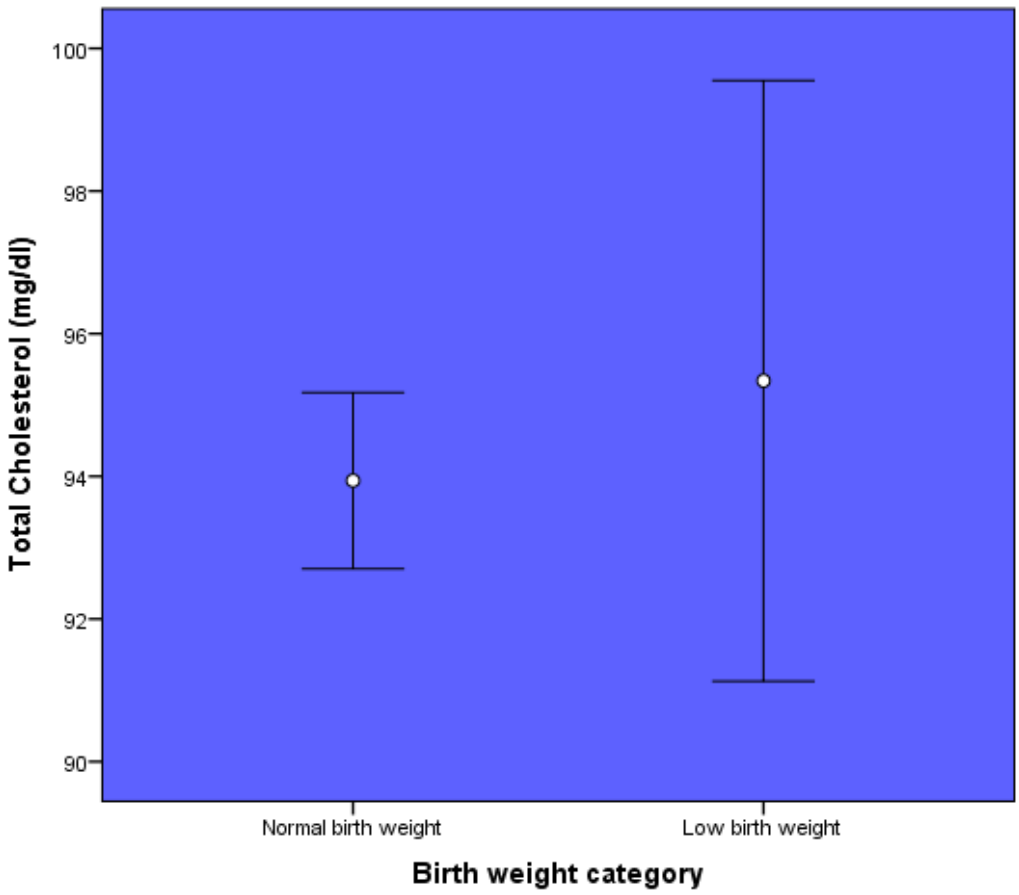
Table 5

Comparison of mean total cholesterol (mg/dl) between birth weight category (N=100)

birth weight category	Total Cholesterol (mg/dl) Mean± SD	Mean difference	95% CI		P value
			Lower	Upper	
Normal birth weight	93.94 ± 4.35	1.40	-2.93	5.73	0.523
Low birth weight	95.34 ± 14.82				

Figure 7

Error bar diagram of comparison of mean total cholesterol (mg/dl)between birth weight category (N=100)



This Diagram shows no significant difference in Cholesterol level in between Normal and Low birth weight babies.

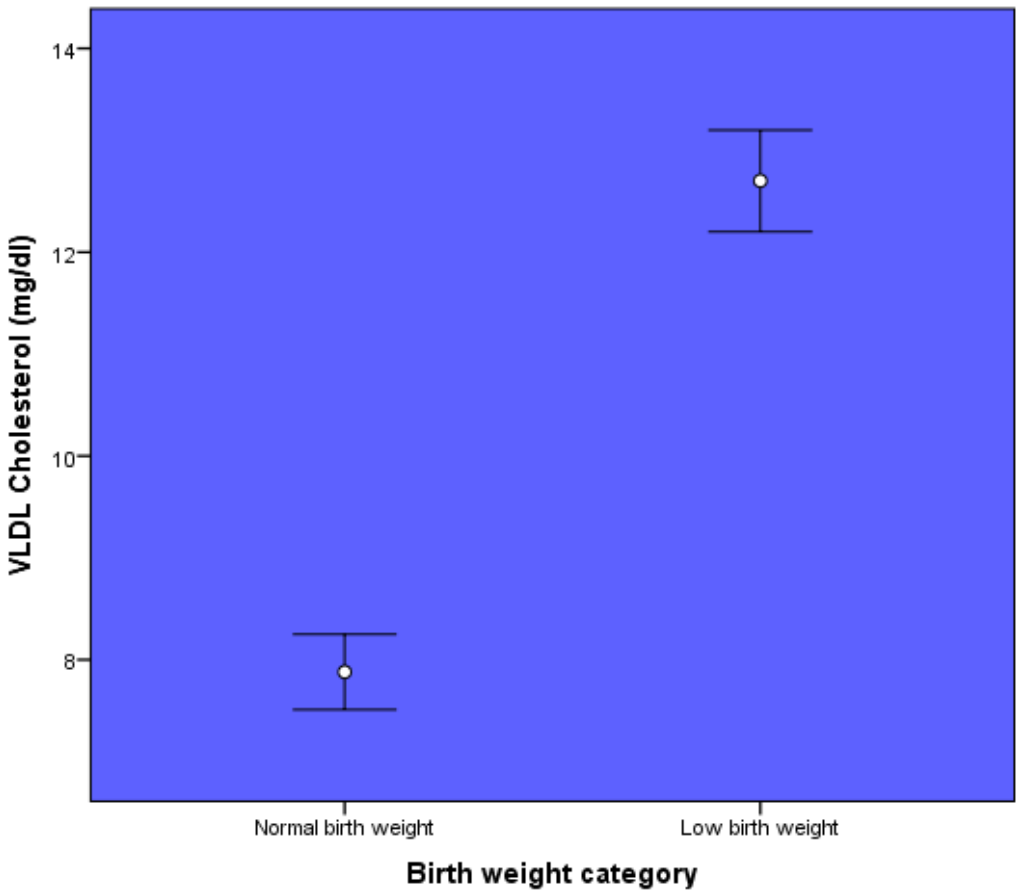
Table 6

Comparison of mean VLDL cholesterol (mg/dl) between study groups (N=100)

Birth weight category	VLDL cholesterol (mg/dl) Mean± SD	Mean difference	95% CI		P value
			Lower	Upper	
Normal birth weight	7.88 ± 1.3	4.82	4.21	5.43	*<0.001*
Low birth weight	12.7 ± 1.75				

Figure 8

Error bar diagram of comparison of mean VLDL cholesterol (mg/dl) between birth weight category (N=100)



This Diagram shows significant difference in VLDL level in between Normal and Low birth weight babies.

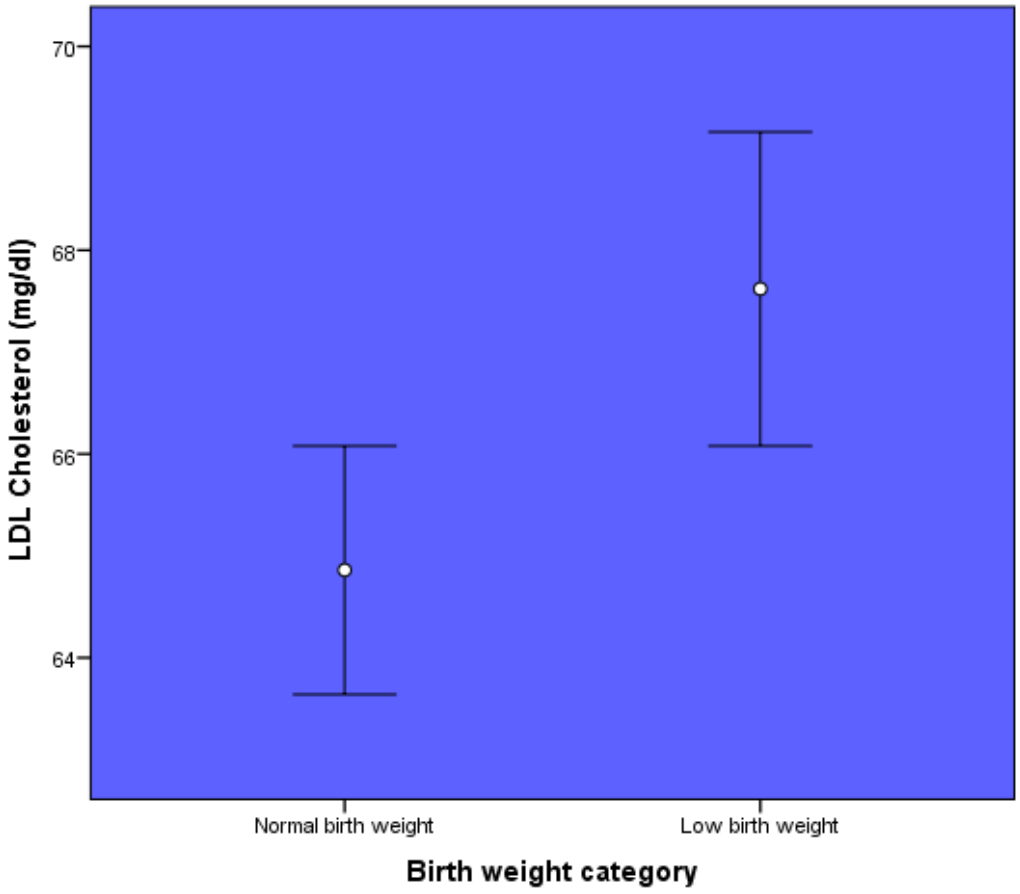
Table 7

Comparison of mean LDL cholesterol (mg/dl) between birth weight category (N=100)

Birth weight category	LDL cholesterol (mg/dl) Mean ± SD	Mean difference	95% CI		P value
			Lower	Upper	
Normal birth weight	64.86 ± 4.29	2.76	0.82	4.70	***0.006***
Low birth weight	67.62 ± 5.42				

Figure 9

Error bar diagram of comparison of mean LDL cholesterol (mg/dl) between birth weight category (N=100)



This Diagram shows no significant difference in LDL level in between Normal and Low birth weight babies.

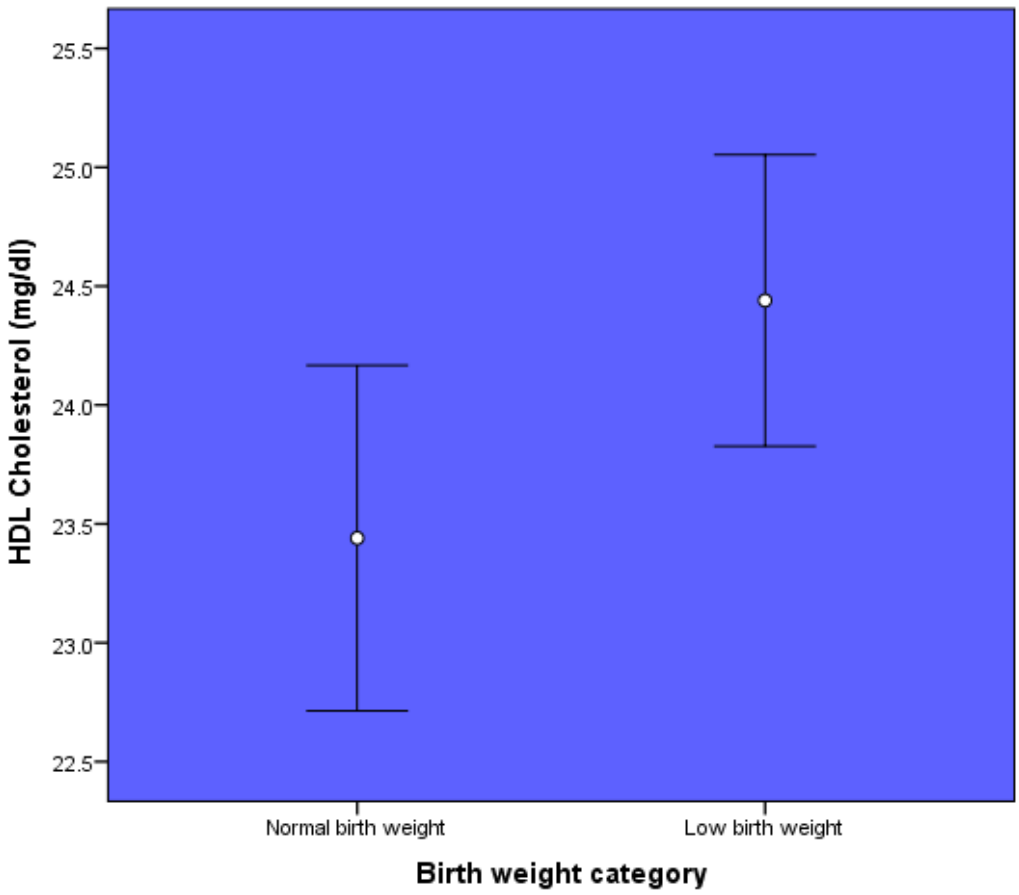
Table 8

Comparison of mean HDL cholesterol (mg/dl) between birth weight category(N=100)

Birth weight category	HDL cholesterol (mg/dl) Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Normal birth weight	23.44 ± 2.56	1.00	0.06	1.94	***0.037***
Low birth weight	24.44 ± 2.16				

Figure 10

Error bar diagram of comparison of mean HDL cholesterol (mg/dl) between birth weight category (N=100)



This Diagram shows no significant difference in HDL level in between Normal and Low birth weight babies.

Table 9

Comparison of gender in study population(N=100)

Gender			Chi square	P-value
	BOYS (N=48)	GIRLS (N=52)		
	48 (48%)	52 (52%)	0.160	0.689

Figure 11

Pie chart of baby gender in the study population (N=100)

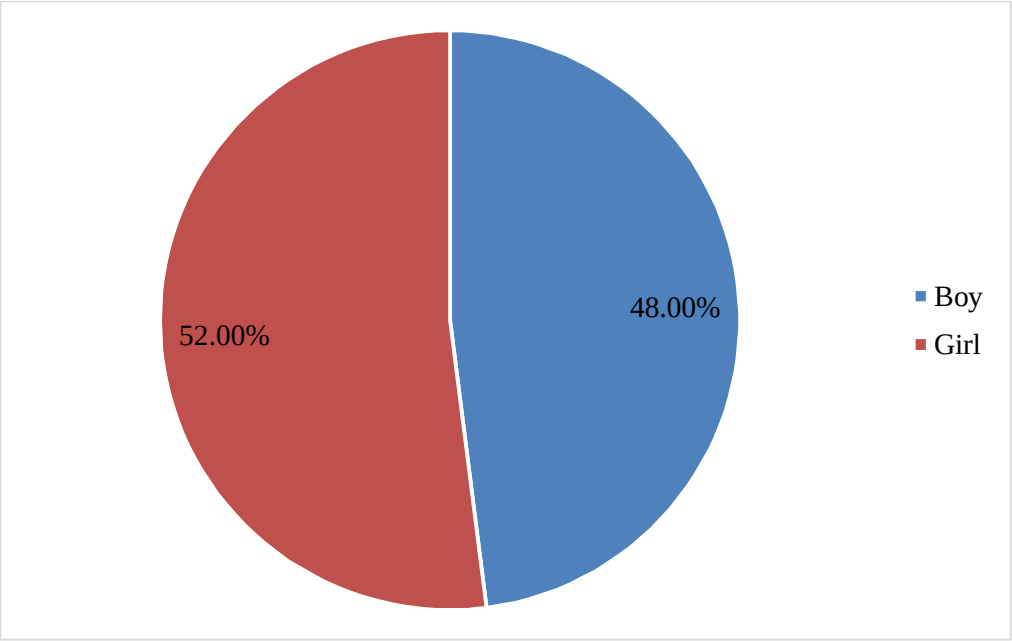


Table 10

Comparison of mean of lipid profile parameters between Boys and Girls (N=100)

Lipid Parameter	Gender		P value
	Boys(N=57)	Girls (N=43)	
Triglycerides (mg/dl)	52.99 ± 11.48	52.25 ± 12.73	*0.790*
Total Cholesterol (mg/dl)	94.08 ± 12.06	96.42 ± 5.65	*0.362*
HDL Cholesterol (mg/dl)	23.84 ± 2.33	24.25 ± 2.66	*0.472*
LDL Cholesterol (mg/dl)	66.71 ± 5.18	64.75 ± 4.43	*0.098*
VLDL Cholesterol (mg/dl)	10.5 ± 2.69	9.63 ± 3.36	*0.194*

The mean triglycerides of Boys group was 52.99 ± 11.48(mg/dl)and 30 Girls group was 52.25 ± 12.73(mg/dl), and the mean difference between two groups was statistically not significant (P value0.790). The mean Total Cholesterol of Boys group was 94.08 ± 12.06(mg/dl)and Girls group was 96.42 ± 5.65(mg/dl), and the mean difference between two groups was statistically not significant (P value 0.362). The mean HDL Cholesterol of Boys group was 23.84 ± 2.33(mg/dl)and Girls group was 24.25 ± 2.66(mg/dl), and the mean

difference between two groups was statistically not significant (P value 0.472). The mean LDL Cholesterol of Boys group was 66.71 ± 5.18(mg/dl)and Girls group was 64.75 ± 4.43(mg/dl), and the mean difference between two groups was statistically not significant (P value 0.098). The mean VLDL Cholesterol of Boys group was 10.5 ± 2.69(mg/dl)and Girls group was 9.63 ± 3.36(mg/dl), and the mean difference between two groups was statistically not significant (P value0.194). (Table 8)

Table 11

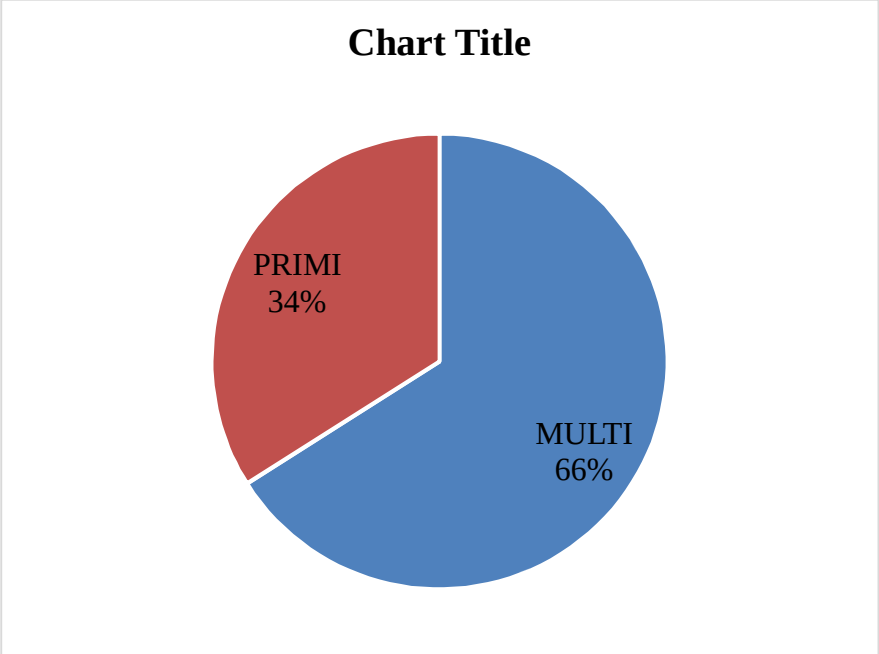
Descriptive analysis of gravida in study population (N=100)

Gravida	Frequency	Percentage
Primi	34	34.00%
Multi	66	66.00%

Among the study population, 34% women participants had primi gravida and 66% women participants had multi gravida. (Table 5).

Figure 12

Pie chart of gravida in study population (N=100)



This pie chart showing 34 primi, 66 multi New Born babies are studied in this group.

Table 12

Comparison of mean of lipid profile parameters between gravida groups (N=100)

Parameter	Gravida		P value
	PRIMI (N=34)	Multi (N=66)	
Triglycerides (mg/dl)	52.32 ± 12.02	53.06 ± 11.66	*0.768*
Total Cholesterol (mg/dl)	95.65 ± 5.91	94.12 ± 12.73	*0.510*
HDL Cholesterol (mg/dl)	24.06 ± 2.21	23.88 ± 2.51	*0.725*
LDL Cholesterol (mg/dl)	67.79 ± 3.96	65.44 ± 5.39	*0.027*
VLDL Cholesterol (mg/dl)	10.47 ± 2.98	10.2 ± 2.83	*0.654*

The mean triglycerides of primi gravida group was 52.32 ± 12.02 (mg/dl) and multi gravidagroup was 53.06 ± 11.66 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.768). The mean total cholesterol of primi gravida group was 95.65 ± 5.91 (mg/dl) and multi gravidagroup was 94.12 ± 12.73 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.510). The mean HDL Cholesterol of primi gravida group was 24.06 ± 2.21 (mg/dl) and multi gravidagroup was 23.88 ± 2.51 (mg/dl), and the mean difference between two groups was statistically not

significant (P value 0.725). The mean LDL Cholesterol of primi gravida group was 67.79 ± 3.96 (mg/dl) and multi gravidagroup was 65.44 ± 5.39 (mg/dl), and the mean difference between two groups was statistically significant (P value 0.027). The mean VLDL Cholesterol of primi gravida group was 10.47 ± 2.98 (mg/dl) and multi gravidagroup was 10.2 ± 2.83 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.654) (Table 7).

Table 13

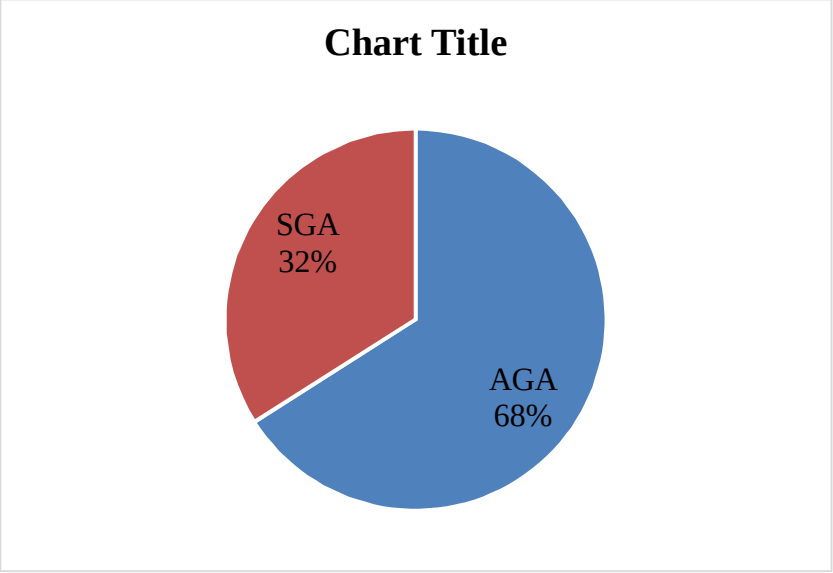
Descriptive analysis of AGA vs SGA in study population (N=100)

	Frequency	**Percentage**
AGA	68	68.00%
SGA	32	32.00%

Among the study population, 68% neonates came under AGA category and 32% neonates acme under SGA category.. babies are categorized in groups by use of AIIMS intrauterine growth charts.

Figure 13

Pie chart of AGA vs SGA in study population (N=100)



This pie chart showing 32 SGA, 68 AGA New Born babies are studied in this group.

Table 14

Comparison of mean of lipid profile parameters between AGA and SGA category (N=100)

lipid profile Parameter	Birth weight category		P value
	AGA (N=68)	SGA (N=32)	
Total Cholesterol (mg/dl)	91.94 ± 4.35	96.34 ± 14.82	*0.523*
Triglycerides (mg/dl)	40.72 ± 7.38	64.9 ± 8.43	*<0.001*
HDL Cholesterol (mg/dl)	24.44 ± 2.56	22.44 ± 3.16	*0.037*
LDL Cholesterol (mg/dl)	62.86 ± 4.29	64.62 ± 5.42	*0.006*
VLDL Cholesterol (mg/dl)	7.88 ± 1.3	8.74 ± 1.75	*0.009*

The mean triglycerides of AGA group was 40.72 ± 7.38 (mg/dl) and SGA group was 64.9 ± 8.43 (mg/dl), and the mean difference between two groups was statistically significant (P value *<0.001)*.

The mean total cholesterol of AGA group was 91.94 ± 4.35 (mg/dl) and SGA group was 96.34 ± 14.82 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.523). The mean HDL Cholesterol of AGA group was 24.44 ± 2.56 (mg/dl) and SGA group was 22.44 ± 3.16 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.037).Here the HDL cholesterol level was low in SGA babies. The mean LDL Cholesterol of

AGA group was 62.86 ± 4.29 (mg/dl) and SGA group was 64.62 ± 5.42 (mg/dl), and the mean difference between two groups was statistically significant (P value 0.006). The mean VLDL Cholesterol of AGA group was 7.88 ± 1.3 (mg/dl) and SGA group was 8.74 ± 1.75 (mg/dl), and the mean difference between two groups was statistically not significant (P value 0.009) (Table 7).

DISCUSSION

Recently interest in cord lipids has increased because serum lipid disorders have their roots in childhood and atherogenic changes are postulated to originate early in life.

Lipid profile is a marker of an underlying cardiovascular status, and there is direct correlation between the abnormalities in lipid profile and occurrence of cardiovascular morbidities and mortality.

Levels of Lipids and Lipoproteins in the cord sera should be a reflection of the status of plasma lipid metabolism in the infant at birth because most fetal Lipids are synthesized de novo through the conversion of glucose to various fatty acid containing compounds. Only part of it is derived from placental circulation, so measurement of cord blood Lipid profile will be like measuring Lipid metabolism during fetal life and at birth.

Among various factors theorised in the development of atherosclerosis, increased plasma levels of cholesterol and/or triglycerides are considered to be most important. Furthermore a number of investigators now consider only LDL and HDL as major risk factors on the development and progression of atherosclerotic vascular diseases.

Hence determinations of cord lipid profile becomes a useful tool in the earlier detection of babies at a higher risk, since several investigators believe that the atherosclerotic lesions may have its genesis in childhood.

There are many studies showing direct relationship between the abnormalities in lipid profile among the preterm and SGA neonates and occurrence of cardiovascular diseases. The present study was undertaken for early detection of abnormalities in the lipid profile at the earliest (at birth), especially in the preterm and SGA neonates, so that these high risk babies can be under vigilant monitoring in future.

Table 15

Comparision Of Influence Of Gender On Neonate Cord Blood Lipid Profile

LIPID PROFILE	PRESENT STUDY		JAGADISH SINGH ET AL		BADIEE Z ET AL		KHALID MIRZA ET AL	
	BOY	GIRL	BOY	GIRL	BOY	GIRL	BOY	GIRL
Total cholesterol	**94.08**± 12.06	**96.42**± 5.65	88.70± 19.1	91.10± 17.2	75.20± 21.1	81.40 ± 8.10*	166.03± 06.99	166.80± 06.64 *
Triglycerides	**52.99**± 11.48	**52.25**± 12.73	-	-	61.00± 02.0	62.00 ± 2.00	56.30±0 6.83	59.29± 06.16
HDL	**23.84**± 2.33	**24.25**± 2.66	-	-			-	-
LDL	**66.71**± 5.18	**64.75**± 4.43	-	-	32.10±16 .30	35.90 ± 2.40	-	-
VLDL	**10.50**± 2.69	**9.63**± 3.36	-	-	28.80±08 .70	31.18 ± 9.97*	74.68±0 7.11	75.14 ± 05.83 *

As per the table shown above in the present study among males and females the cord lipid profile values were approximately equal with no statistically significant p value.

Similar observations were made by Jagadish Singh et al.[26] but in Badiee z et al.[31] Khalid Mirza et al.[92] Female neonates had significantly higher TC and HDL (p=<0.05, p=<0.05 respectively), but LDL value was higher in females but it was not statistically significant.

TABLE 16

COMPARISION OF INFLUENCE OF BIRTH WEIGHT OF NEONATE ON CORD LIPID PROFILE

Lipid profile	**Present study**		**A Kalra et al study**		**N.Haridas and P.T. Acharya et al**		**Jagadish singh et al Study**	
Birth weight	NBW >2.5 kg	LBW <2.5kg	NBW	LBW	NBW	LBW	NBW	LBW
Total cholesterol	**93.94**± 4.35	**95.34**± 14.82	**76.6** ± 24.4	**67.8**± 10.8	**90.0**± 20.2	**95.00** ± 20.2	**96.5**± 15.1	**69.5**± 10.9
Triglycerides	**42.72**± 5.38	**62.90**± 6.43	**-**	**-**	**45.0**± 13.8	**59.1**± 22.30	**-**	**-**
VLDL	**7.88**± 1.30	**12.70**± 1.75	**-**	**-**	**-**	**-**	**-**	**-**
LDL	**64.86**± 4.29	**67.62**± 5.42	**20.7**± 5.8	**19.5**± 0.7	**-**	**-**	**-**	**-**
HDL	**23.44**± 2.56	**24.44**± 2.16	**22.5**± 6.5	**20.5**± 7.3	**-**	**-**	**-**	**-**

As per the table shown above in the present study LOW birth weight babies had significantly elevated lipid parameters such as Total cholesterol, Triglycerides, LDL, HDL, VLDL but TG and VLDL values only statistically increased ($P<0.005$) in LOW birth weight babies than NORMAL birth weight babies.

N.Harias and P.T.Acharya et al.[15] in their study concluded that Low birth weight neonates have higher TG and TC levels but statistically significant difference was found only in TC ($p<0.001$) levels.

Mathur et al.[16] in their study concluded that in Low birth weight neonates, TC value was significantly high ($p<0.001$).

Jane Oba et al.[28] in their study concluded that TC, LDL, HDL values were significantly higher in Low birth weight neonates ($p<0.0001$), TG value was significantly higher in Low birth weight neonates ($p<0.01$).

Pardo et al.[11] in their study concluded that TC, LDL, HDL were higher in Low birth weight neonates compared to Normal birth weight neonates with statistically significant difference in TC and LDL ($p<0.001$) levels, but HDL had no statistically significant difference. AI values were more in low birth weight compared to normal babies which was not statistically significant.

A K Kalra et al.[17] in their study concluded that all Cord lipid profile values were lower in low birth weight neonates compared to normal birth weight neonates but statistically significant difference was found with TC levels ($p <0.001$) and no statistically significant difference was found with HDL and LDL levels.

Jagadish Singh et al.[26] in their study concluded that normal neonates had higher TC compared to low birth weight neonates with statistically significant difference ($p<0.05$).

Table 17

Comparision Of Influence Of Birth Weight (Aga Vs Sga) Irrespective Of Gestational Age Of Newborn On Cord Blood Lipid Profile

Lipid Profile	Present study		Tejasree katragadda Et al study		Jane Oba et al Study		Ajay Kumar et al. Study	
	AGA	SGA	AGA	SGA	AGA	SGA	AGA	SGA
TC (mg/dl)	91.94 ± 4.35	96.34 ± 14.82	85.4± 22	83.6± 31.6	57±19	57±19	85.83± 22.85	92.2± 8.32
TGL (mg/dl)	40.72 ± 7.38	64.9 ± 8.43	55.5± 26	74.5± 39.9	42±25	42±25	35.27± 17.49	104.5± 20.8*
HDL (mg/dl)	24.44 ± 2.56	22.44 ± 3.16	36.3± 12	32.5± 13.3	30±14	30±14	-	-
LDL (mg/dl)	62.86 ± 4.29	64.62 ± 5.42	39.6± 5	38.8± 23.8	19±8	19±8	-	-
VLDL (mg/dl)	7.88 ± 1.3	8.74 ± 1.75	-	-	-	-	-	-

AGA – Appropriate for gestational age

SGA- Small for gestational age

As per table shown above, in present study in SGA neonates cord blood Triglycerides, Total cholesterol, LDL, VLDL levels were elevated and HDL levels were decreased compared to AGA neonates. But statistically only Triglycerides level alone elevated in SGA babies (P<0.005).. This can be explained on the fact that Triglyceride and VLDL, its synthesis is increased in SGA babies and also its metabolism is decreased due to decreased activity of lipoprotein lipase.[23]

Jane Oba et al.[28] in their study they concluded that Preterm SGA had higher values of TC, TG, LDL, HDL compared to Preterm AGA which was statistically significant with P values <0.0001, <0.01, <0.0001, <0.0001 respectively and Term SGA had higher values of TC, TG, LDL, HDL compared to term AGA which was statistically significant with P values <0.0001, <0.01, <0.0001,<0.0001 respectively.

Ajay Kumar et al.[19] in their study they concluded that Term AGA and Preterm AGA had higher values of TC compared to Term SGA and Preterm SGA but values were not statistically significant. Term SGA and Preterm SGA had higher TG value compared to Term AGA and Preterm AGA values which were statistically significant (p=<0.05).

Tejasree katragadda et al study in their they found that SGA babies had elevated lipid parameters with statistically significant values in Triglycerides.

Low birth weight infants are born with intra uterine malnutrition .Such circumstances favour fetal adipose tissue break down liberating free fatty acids, which escapes oxidation for energy, is synthesized in the liver into triglyceride, which causes elevated levels of Triglyceride in low birth weight babies .Intrauterine malnutrition could be result of placental insufficiency.[19]

The prevalent concept is, having bad habits in adult life, such as being sedentary, eating a high fat diet and smoking cause coronary heart disease .The fetal hypothesis does not deny the importance of these adult factors , it simply adds another layer to the complex and multifactorial etiology of the disease, suggesting that in addition to genetic factors and life style factors fetal nutrition needs to be considered a risk factor. There have been studies to show that coronary heart disease has its roots traceably to infancy. Hyperlipoprotenemia at birth is one of the risk factors for developing coronary artery disease later in life.[28]

In our study there is an increase in the cord blood levels of Total Cholesterol in preterm newborns and an elevated TG levels in low birth weight newborns. This suggests that a fetus receiving inadequate nutrition has to make adaptations in order to survive and may be prone to hyperlipidemia. Thus strategy to prevent coronary heart disease must include measures to improve fetal growth and early detection of hyperlipidemia with dietary intervention during infancy and later childhood.

In the present study cord blood lipid profile values in SGA were elevated when compared to AGA, the reason is that, there is lack of glucose as fuel in SGA babies, so these babies use alternative source as a fuel (amino acid and lipids) and generate glucose (gluconeogenesis), where by activating lipid and other metabolism, so there will be increased hepatic generation of lipids (particularly VLDL and chylomicrons) also, there is decreased peripheral utilization of lipids because of decreased activity of lipoprotein lipase enzyme in growth restricted babies, these two facts explain higher concentration of plasma lipids in SGA babies.[9,11,]

Barker hypothesis demonstrated that low birth weight correlated with an increased prevalence of Cardiovascular disease, hypertension and type 2 diabetes mellitus and suggested that this association reflects the phenomenon known as programming, whereby a stimulation or insult during a critical period of intrauterine life could also result in alterations of physiology and metabolism during adult life.

So those born with low weight at birth need more follow up in their latter life.

CONCLUSIONS

The following conclusions were drawn from this study:

GENDER:

There was no statistically significant difference in cord lipid profile between males and females in both term and preterm neonates.

BIRTH WEIGHT:

Cord blood Lipid profile values for TG, and VLDL were significantly higher ($P<0.005$) in low birth weight babies compared to normal birth weight babies.

Cord blood lipid profile values for TC, HDL and LDL were not significantly higher in low birth weight babies.

AGA/SGA:

Cord blood lipid profile values for TG was significantly higher in SGA babies $P<0.005$ compared to AGA babies.

SUMMARY

The objective of the present study was to know the abnormalities in the cord blood lipid profile values in low birth weight neonates compared to normal birth weight neonates as well as SGA neonates compared to AGA neonates.

After taking written informed consent, relevant maternal data was collected; cord blood was collected immediately after the delivery, blood was allowed to clot for separation of the serum and then sent to lab for further analysis. The babies were examined and all relevant anthropometric variables were recorded and then babies were classified into NORMAL and LOW BIRTH WEIGHT based on birth weight, SGA or AGA group with the use of AIIMS Intrauterine growth charts and Ponderal index.

This hospital based case control study was conducted from March 2018 to august 2018 enrolling 100 neonates of which 50 babies were above 2.5 kg and 50 were below 2.5 kg..Of which 48 were boys and 52 were girls. Out of 100 neonates, 68 were AGA, 32 were SGA.

Majority of the neonates in our study were females (52%).. Among AGA, male neonates were more (60.2%) and among SGA, female neonates were more (48.5%) but there was no statistically significant difference in gender distribution amongst any groups.

Cord lipid profile values were higher in LOW birth weight neonates compared to NORMAL birth weight neonates.

Cord lipid profile values were higher in SGA neonates compared to AGA neonates except for HDL (32.77±09.57), which was lower in SGA neonate.

Cord lipid profiles values in LOW birth weight neonates were – TG (62.9 ± 6.43), TC (95.34 ± 14.82), HDL(24.44 ± 2.16), LDL(67.62 ± 5.42), VLDL (12.7 ± 1.75). Cord lipid profiles values in NORMAL birth weight neonates – TC (93.94 ± 4.35), TG (42.72 ± 5.38), HDL (23.44 ± 2.56), LDL (64.86 ± 4.29), VLDL (7.88 ± 1.3).In Cord lipid profile values total cholesterol and VLDL values were higher in LOW birth weight neonates compared to NORMAL birth wight neonates, which were statistically significant ($P<0.005$).

Cord lipid profile values in SGA neonates were – TC (96.34±14.82), TG (64.9±8.43), HDL(22.44±3.16), LDL(64.62±5.42) VLDL (8.73±1.75). Cord lipid profile values in AGA neonates were – TC (91.94±4.35), TG (40.72±7.38), HDL (24.44±2.56), LDL (62.86±4.29), VLDL (7.88±1.33). Cord lipid profile values Triglycerides were higher in SGA neonates which were statistically significant ($p<0.005$) compared to AGA neonates.. HDL level was lower in SGA neonate but statistically not significant.

BIBLIOGRAPHY

1. Anderson GE Friis Hansen B. Cord serum lipid and lipoprotein cholesterol values in normal and lowbirth weight neonates 1977 ; 66: 355-360.

2. Ginsburg BE Zettersotrom R.Serum cholesterol concentrations in newborn infants with gestational ages of 28 to 42 weeks. Acta Pacdiartr stand 1980; 69: 587- 592.

3. Carr BR Parker CR Jr Milewich L et al the role of low density.high density and very low density lipoproteins in steroidogenesis 1980 ; 106: 185& 1860.

4. Parker CR Jr Simpson ER , Bilheimer DW et al Inverse relation between low density lipoprotein, cholesterol, in human foetal plasma 1980 ; 208: 512_514.

5. Glueck CJ , Heckman F, schoenfeld M, et al Neonatal familial type 2 hyper lipoproteinemia; cord blood cholesterol in 1800 births. Metabolism 1971 ; 20: 597- 608.

6. Harding PGR . The metabolism of brown and white adipose tissue in the foetus and newborns clinic Obstetrics gynecology 1971; 4 685- 709.

7. Tsang RC, Glueck CJ, Evans G, Steiner P Cord blood hypertriglyceridemia Am J Dis Child 1974; 127: 78- 82.

8. Pushpendra Magon . R.S. Bharatwaj, Manorama Verma, Jugesh Chatwal. Cord blood lipid profile at birth among normal newborns and its relationship to birth weight.indian journal of research 2013 ; 2(7): 2250- 1991.

9. Donega S Oba J Maranhao RC Concentration of serum lipids and apolipoproteins in newborns Arq Bras Cardiol 2006 ; 86:419- 424.

10. Sreekarthick KP, Shuba Jayaram, Aravind Karinagannanavar, Sumana Sindhuram V ; A Study of cord blood lipid profile in preterm and term neonates IJAR 2015; 1(8): 276- 281.

11. A joint statement by the American Heart Association .The Cholesterol Facts. Circulation 1980,81.

12. Glueck CJ, Tsang RC. Pediatric type –II hyperlipoprotenemia. Effect of diet on plasma cholesterol in the first year of life .Am J Clin Nutr 1972,25:224- 230.

13. Berenson G S, Blonde CV ,Farris RP, Foster TA ,Frank GC, Srinivasan SR,Voors AW, Webber LS .Cardiovascular disease risk factor variables during the first year of life .Am J Dis Child 1979 ,133:1049-1058.

14. Lauer RM ,Connor WE, Leaverton PE, Reiter NA, Clake MS. Coronary heart disease risk factors in school children: The Muscatine study J Pediatr 1975,86:697-706.

15. Kent L, Thornburg. Fetal Origins of Cardiovascular Disease. American Academy of Pediatrics December 2004; (5): 527-34.

16. Sawant AM, Shetty D, Mankeshwar R, Ashavaid TF Prevalence of dyslipidemia in young adult Indian population. J Assoc Physicians India. 2008 Feb;56:99-102.

17. Meenakshi Sharma,Nirmal Kumar Ganguly , Premature coronary artery disease in Indians and its associated risk factors, Vascular Health and Risk Management 2005:1(3) 217–225, 2005 Dove Medical Press Limited.

18. Rasa Verkauskiene, Paul Czernichow, Claire L M. Long-term metabolic consequences of being born small for gestational age. Expert Review of Endocrinology and Metabolism May 2006; (1): 439-447.

19. Jones J N, Taylor Gercel, Taylor Doughlas D. Altered cord serum lipid levels associated with small for gestational age infants. Journal of American College of Obstetricians and Gynecology Oct 1999; 93: 527-531.

20. Molina M, Casnueva V, Cid X, Chiang MT, Ferrada MC, Perez R, et al. Lipid profile in newborns with intrauterine growth retardation. Rev Med Chil 2000 July; 128 (7): 741-748.

21. I.M.C.G.Pardo,B Geloneze, M A Tambascia, A A Barros Filho. Atherogenic lipid profile of Brazalian near term newborns. Brazilian Journal of Medical and Biological Research May 2005; 38(5): 755-760.

22. Hossain MA, Islam MN, Shahidullah M , Akhter H. Serum triglyceride level in IUGR babies and its comparison with preterm AGA and term normal babies. Mymensingh Med J. 2006 Jul; 15(2): 180-182.

23. Daniel M. Lane and walter J. Mcconathy. Factors affecting the lipid and Apolipoprotein levels of cord sera. Pediatr. Res 1983; 17: 83-91.

24. Misra PK ,Tiwari DK, Sharma B,Kaul R.Free fatty acids and Triglycerides in normoglycemic low birth weight newborns in early neonatal period. Indian J Pediatr 1984, 51:637-641.

25. Haridas N, Acharya PT. Serum Lipid Status in neonates. Indian Pediatr 1984, 21:327-334.

26. Mathur PP , Prasad R, Jain SK, Pandey DH,Singh SP. Cord blood Cholesterol in term and preterm newborns. Indian Pediatr 1986,23:103-106.

27. Kalra A ,Kalra K, Agarwal MC, Prasad R, Pant MC ,Bhatia R, Mittal R.Serum lipid profile in term and preterm infants in early neonatal period .Indian Pediatr 1988,25 :977-981.

28. Dogra J, Sengar GS, Mathur HC ,Misra SN. Serum lipids in neonatal cord blood in families with diabetes mellitus Type-1. Indian Pediatr 1988, 25:267- 271.

29. Kumar A ,Gupta A, Malhotra VK ,Thirupuram S,Gaind B,Cord blood lipid levels in low birth weight newborns .Indian Paediatr,1989,26,571-574.

30. Van-der-schouw YT, ALMD, Hornstra G, Bullstraw, Ramkers MT, Huisjes HJ.Fattyacids composition of serum lipids of mother and their babies after normal and hypertensive pregnancies. Prostaglandins-Leucot-Essent-Fatty-acids.1991,44:247- 252.

31. Kherkeulidze P, Johansson J, Carlson LA .High density lipoprotein particles size distribution in cord blood .Acta Paediatr Scand 1991,80:770-779.

32. Averna MR , Barbagallo CM , Dipaola G , Labisi M , Pinna G, Marino G, Dimita U , Notarbartolo A. Total cholesterol ,IDL – Cholesterol and lipoprotein B in umbilical cord blood: cross sectional study .Minerva-Pediatr 1992,44:395-399.

33. Xinli Wang, Yunpu Cui, Xiaomei Tong, Hongmao Ye, Song Li. Glucose and Lipid metabolism in Small for gestational age infants. The Journal of Clinical Endocrinology & Metabolism Feb 19 92; (2): 681–684.

34. Averna MR, Barbagallo CM ,Di-paola G, La-Placa FP , Scafidi V, Dimita U, Notarbartoloa A. Transient Neonatal Hypercholesterolemia, Lack of relationships with dehydroepiandro sterone sulphate .Horm-Metab-Res 1993,25:271-274.

35. Barker D J P, Martyn C N, Osmond C, Hales C N, Fall C H D. Growth in utero and serum cholesterol concentrations in adult life. BMJ 1993; 307: 1524- 72.

36. Jagdish Singh, Mira Purohit, Puspha Singh, D.M. Thappa. Cord Blood Cholesterol in Term and PreteTerm Newborns. Indian Pediatr. Oct 94; (31): 1278-80.

37. Claire Levy-Marchal and Delphine Jaquet. Long-term metabolic consequences of being born small for gestational age. Pediatric Diabetes Sep 2004; (5)3: 147-153.

38. Jane Oba, Sirlei Donega, Raul C, Maranhao.Concentration of serum lipids and Apolipoprotein B in Newborn; Arquivos Brasileiros de cardiologia: volume86,N(6),June 2006.

39. Kelishadi R, Badiee Z, Adeli K. Cord blood lipid profile and associated factors: baseline data of a birth cohort study. Paediatric and Perinatal Epidemiology 2007; 21: 518 -524.

40. Cristina Catarino, Irene Rebelo, Luís Belo, Petronila Rocha-Pereira, Susana Rocha, Elisabeth Bayer Castro et al. Fetal lipoprotein changes in pre- eclampsia. Acta Obstetricia et Gynecologica Scandinavica 2008; (87)6: 628- 634.

41. Badieez, Kelishadir. Cord lipid profile in a population of Iranian term newborns. Pediatr cardiol. 2008 May;29(3):574-579.

42. Ortem JM, Neuhans OW,Biochemistry 8th ed. St.Louis:1980,269-337.

43. Boultan T J C. Serum cholesterol in early childhood . Acta Paediatr Scand 1980, 69:441-445.

44. Peter A. Mayes and Kathleen M. Botham. Lipids of Physiologic Significance Chapter 14 in: Robert K. Murray, Daryl K. Granner, Peter A. Mayes and victor W. Rodwell. Harper's illustrated Biochemistry 26th edition, Lange publication, 2003; pp 205-218.

45. William A. Neal. Disorders of Lipoprotein Metabolism and Transport Chapter 86.3 in: Kliegman MR, Behrman RE, Jenson

HB, Stanton BF. Nelson Textbook of Pediatrics, 18th Edition. Philadelphia (USA): Elsiever; 2007, pp 580-593.

46 .Mizra K, Ahmed P, Bilgrami NL, Ullah MS , Lipids and lipoprotein values in normal children .Indian Pediatr 1984 , 21 :313-317.

47 Connar SL, Connar WE, Sexton G, Calvin L, Bacon S. The effects of age, body weight and family relationships on plasma lipoproteins and lipids in men, women and children of randomly selected families .Circulation 1982,65:1290-1298.

48. Ramakrishna S,Prasanna KG ,Rajan R,text book of medical biochemistry 2nd ed. Chennai :orient langman ltd,1989,209-244.

49. Kumar A ,Gupta A, Malhotra VK ,Thirupuram S,Gaind B,Cord blood lipid levels in low birth weight newborns .Indian Paediatr,1989,26,571-574.

50. Robert WC, Ferrans VJ,Levy RI ,Fredrickson DS.Cardivascular pathology in hyperlipoprotenemia.Am J Cardiol 1973,31:557-570.

51. Kumar K,Anand NK, Janah S. Serum lipid profile in children of parents with coronary artery diseases Indian Paediatr,1979 ,16:1107-1113.

52. Tsang R, Glueck CJ,Evans G, Steiner PM ,Cord blood hypertriglyceredemia AM J Dis Child 1974,127:78-82.

53. Dogra J, Sengar GS, Mathur HC ,Misra SN. Serum lipids in neonatal cord blood in families with diabetes mellitus Type-1. Indian Pediatr 1988, 25:267- 271.

54. Tsang R C, Fallat R W, Glueck C J. Cholesterol at birth and age 1, Comparison of normal and hypercholesterolemic neonates. Pediatrics 1974, 53:458-470.

55. Haridas N, Acharya PT. Serum Lipid Status in neonates. Indian Pediatr 1984, 21:327-334.

56. Misra PK ,Tiwari DK, Sharma B,Kaul R.Free fatty acids and Triglycerides in normoglycemic low birth weight newborns in early neonatal period. Indian J Pediatr 1984, 51:637-641.

57. Goel BK. Routine biochemical tests. In a procedure manual for routine diagnostic test .Mukherjee KL(Editor).New Delhi :Tata-McGraw-Hill publishing company limited .,1988,985-1079.

58. Jaffe D, Hartcroft WS ,Manning M, Eleta G. Coronary arteries in new born children. Acta Paediatr Scand 1971,Supp:219.

59. G Steiner, L Schwartz, S Shumak and M Poapst. The association of increased levels of intermediate-density lipoproteins with smoking and with coronary artery disease. Journal of American Heart Association *Circulation* 1987, 75:124-130.

60. Kannel WB, Castelli WP , Gordont. Chlosterol in the prediction of atherosclerotic disease: New perspective based on the Framingham study .Am Interim Med 1979,90:85-91.

61. Kannel WB , Dawber TR. Atherosclerosis as a pediatric problem. J Pediatr 1972,80:544-554.

62. Kherkeulidze P, Johansson J, Carlson LA .High density lipoprotein particles size distribution in cord blood .Acta Paediatr Scand 1991,80:770-779.

63. Daniel M. Lane and walter J. Mcconathy. Factors affecting the lipid and Apolipoprotein levels of cord sera. Pediatr. Res 1983; 17: 83-91.

64. Kimura RE. Lipid metabolism in the fetal-placental unit. In Principles of Perinatal-Neonatal Metabolism . Cowett RM(Editor). Newyork: Springer- Verlag NewYork Inc.,1991,291-303.

65. Dancsi T, Molnar D ,Klujber L. Lipid levels in very low birth weight infants. Acta Paediatr Scand 1990,79:577-580.

66. Thomas CR.Placental transfer of non esterified fattyacids in normal and diabetic pregnancy. Biol Neonates 1987,51:94-104.

67. Ziegler E E, Fomon S J, Haschke F, Nelson S E. Body composition of reference children from birth to age 10 years. Am J Clin Nutr 1982;35:1169- 1175.

68. A Montes, CE Walden, RH Knopp, M Cheung, MB Chapman and JJ Albers. Physiologic and supraphysiologic increases in lipoprotein lipids and apoproteins in late pregnancy and postpartum. Possible markers for the diagnosis of "prelipemia". Journal of American Heart Association. *Arterioscler Thromb Vasc Biol* 1984, 4:407-417.

69. Hendrickse W, Stammers J P, Hull D. The transfer of free fatty acids across the human placenta. Br J Obstet Gynaecol. 1985 Sep;92(9):945-52.

70. Elphick M C, Hull D. The transfer of free fatty acids across the rabbit placenta. J Physiol (1977), 264, 11;pp.751-766.

71. Thomas C R, Lowy C. Placental transfer of free fatty acid: factor affecting transfer across the guinea – pig placenta. J Dey physiol, 1983 Oct; 5 (5):323- 332.

72. Hershfield MS, Nemeth AM. Placental transport of free palmitic and linoleic acids in the guinea pig. J Lipid Res. 1968 Jul;9(4):460-8.

73. Steven S, Nancy H D, Rudi S. Bilirubin metabolism in fetus. Journal of clinical investigation.1964;Vol.43, no.32-39.

74. Barker DJP. Fetal origins of coronary heart disease. Br Med J 1995; 311: 171- 174.

75. Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. Lancet 1989; 2(8663): 577- 580.

76. Frankel S, Elwood P, Sweetnam P, Yarnell J, Smith GD. Birthweight, body- mass index in middle age, and incident coronary heart disease. Lancet 1996; 348: 1478-1480.

77. Leon DA, Lithell HO, Vagero D, Koupilova I, Mohsen R, Berglund L, Lithell UB, McKeigue PM. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915–29. Br Med J 1998; 317(7153): 241-245.

78. Rich-Edwards JW, Stampfer MJ, Manson JE, Rosner B, Hankinson SE, Colditz GA, Willett WC, Hennekens CH. Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976. Br Med J 1997; 315:3 96-400.

79. Stein CE, Fall CHD, Kumaran K, Osmond C, Cox V, Barker DJP. Fetal growth and coronary heart disease in South India. Lancet 1996; 348: 1269- 1273.

80. Barker DJ. The Wellcome Foundation Lecture. The fetal origins of adult disease. Proc R Soc Lond B Biol Sci 1995; 262(1363): 37-43.

81. Roseboom TJ, van der Meulen JH, Ravelli AC, Osmond C, Barker DJ, Bleker OP. Effects of prenatal exposure to the Dutch famine on adult disease in later life: an overview. Twin Res 2001; 4(5): 293-298.

82. Eriksson JG, Forsen T, Tuomilehto J, Osmond C, Barker DJP. Early growth and coronary heart disease in later life: longitudinal study. Br Med J 2001; 322: 949-953.

83. Napoli C, Glass CK, Witztum JL, Deutsch R, D'Armiento FP, Palinski W. Influence of maternal hypercholesterolaemia during pregnancy on progression of early atherosclerotic lesions in childhood: Fate of Early Lesions in Children (FELIC) study. Lancet 1999; 354(9186): 1234-1241.

84. McGarry JD,Takabayashi Y,Foster DW.The role of malonyl-CoA in the coordination of fatty acid synthesis and oxidation in isolated rat hepatocytes . J Bio Chem 1978,253: 8294-8300.

85. Cook G A, King M T, Veech R L .Ketogenesis and malonyl coenzyme A content of isolated rat hepatocytes .J BioChem 1978, 253:2529-2531.

86. Paterson P,Sheath J, Taft P, et al maternal and fetal ketone concentration in plasma and urine.Lancet 1967,1:862-865.

87. Barker D J P, Martyn C N, Osmond C, Hales C N, Fall C H D. Growth in utero and serum cholesterol concentrations in adult life. BMJ 1993; 307: 1524- 72.

88. Physical status: the use and interpretation of anthropometry. Report of a WHO expert committee. WHO Technical Report Series, 1995, 854 : 121 – 60.

89. Fazlul Huque, Zakir Hussain A.M. Detection of low birth-weight new born babies by anthropometric measurements in Bangladesh. Indian Journal of Pediatrics, 1991; 58: 223 – 310.

LIST OF ABBREVIATIONS

AGA	Appropriate for Gestational Age
AI	Atherogenic index
ANC	Ante Natal check up
APOA	Apolipoprotein A
APOB	Apolipoprotein B
ATP	Adenosine
B.Wt	Birth weight
CAD	Coronary artery disease
CHD	Coronary heart disease
COA	Coenzyme A
DM	Diabetes mellitus
EFA	Essential fatty acid
ELBW	Extremely low Birth weight
FFA	Free fatty acid
GA	Gestational age
HC	Head circumference
HDL	High density Lipoproteins
IDL	Intermediate density lipoprotein
IUGR	Intra uterine growth retardation
LBW	Low birth weight

LDL	Low density Lipoproteins
Leng	Length
LGA	Large for Gestational age
LPL	Lipo protein lipase
PE	Pre-eclampsia
PI	Ponderal index
PIH	Pregnancy induced hypertention
PT	Preterm
SD	Standard deviation
SGA	Small for gestational age
T	Term
TC	Total cholesterol
TG	Triglyceride
VLBW	Very low birth weight
VLDL	Very low density lipoprotein

PROFORMA

COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT

- NAME: B/O DATE:
- SEX:
- BIRTH WEIGHT:

ANTENATAL HISTORY:

GRAVIDA: LMP: EDD:

GESTATIONAL AGE:

MATERNAL MEDICAL COMORBIDITIES:

MATERNAL MEDICATIONS:

PERINATAL EVENTS

PROLONGED SECOND STAGE OF LABOUR:

RISK OF SEPSIS:

COLOUR OF LIQUOR:

EVIDENCE OF FOETAL DISTRESS:

NATAL HISTORY

MODE OF DELIVERY:

INDICATION;

(if LSCS)

APGAR:

1 MIN: 5 MIN:

GENERAL EXAMINATION

GESTATIONAL AGE BY BALLORD SCORE:

HR: RR:

LENGTH: HEAD CIRCUMFERENCE:

SYSTEMIC EXAMINATION

CVS:

RS:

P/A:

CNS:

INVESTIGATIONS

1. **TRIGLYCERIDES**
2. **TOTAL CHOLESTEROL**
3. **VLDL**
4. **LDL**
5. **HDL**

SIGNATURE OF THE INVESTIGATOR

SIGNATURE OF THE GUIDE

INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 105/2018 Meeting held on 12.03.2018

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT BABIES" submitted by Dr.S.Prakasam , Post Graduate in Peadiatrics, Government Kilpauk Medical College, Chennai-10

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

6.4.2018

DEAN
Govt. Kilpauk Medical College,
Chennai-10.

6-4-18

ME 1 Sec> Ethical Committee

<u>சுயஒப்புதல்படிவம்</u>

ஆய்வுசெய்யப்படும்தலைப்பு: \¶¯õÚ ©ØÖ® Gøh SøÓÁõÚ £a] Í [SÇ¢øuP Î ß öuõ¨¦Ò öPõi Cµzuzv À, öPõÊ¨¦a \zvøÚ £¶÷\õuøÚ ö\´uÀ

இடம்:பொதுமருத்துவத்துவதுரை

அரசுகீழ்பாக்கம்மருத்துவகல்லூரிமருத்துவமனை

சென்னை

பங்குபெறுபவரின்பெயர் :

பங்குபெறுபவரின்வயது : பங்குபெறுபவரின்எண் :

மேலேகுறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்துகொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதைசார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்கமாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

இடம் :

தேதி :

PATIENT CONSENT FORM

Study detail **"COMPARATIVE STUDY ON UMBILICAL CORD BLOOD LIPID PROFILE BETWEEN NORMAL AND LOW BIRTH WEIGHT "**

Study centre : KILPAUK MEDICAL COLLEGE, CHENNAI

Patients Name :

Patients Age :

Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in

respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

Signature/thumb impression:

Patients Name and Address: place date

Signature of investigator :

Study investigator's Name : place date

S.NO	NAME	BIRTH WEIGHT	AGA/ SGA	SEX	GRAVIDA	LIPID PROFILE				
						TG	TC	VLDL	LDL	HDL
1	B/O THARANI MOHAN	3.2	AGA	GIRL	PRIMI	48	96	9	68	26
2	B/O VANITHA DINESHKUMAR	2.7	SGA	BOY	MULTI	52	92	9	69	25
3	B/O KALAVATHY ILAIYARAJA	2.6	SGA	BOY	PRIMI	42	91	8	65	20
4	B/O MAHALAKSHMI ARUN	3.5	AGA	GIRL	PRIMI	44	99	10	74	26
5	B/O SHANTHI RAGU	3.6	AGA	GIRL	MULTI	36	102	9	72	24
6	B/O REKHA VIJAY	2.8	AGA	GIRL	MULTI	46	92	7	58	27
7	B/O LATHA VIJAYKUMAR	2.84	AGA	GIRL	MULTI	38	90	8	56	21
8	B/O NEEJA VIGNESH	3.5	AGA	BOY	PRIMI	52	86	5	66	24
9	B/O VIJAYA KAMESH	2.64	SGA	GIRL	PRIMI	56	98	9	62	26
10	B/O INDIRA NAGARAJ	2.96	SGA	BOY	MULTI	42	95	8	64	22
11	B/O PRIYA RAMESH	3.1	AGA	BOY	MULTI	46	93	9	68	20
12	B/O NANDHINI PARTHIBAN	3.4	AGA	BOY	MULTI	39	90	7	58	19
13	B/O AISHWARYA SURESH	3.17	AGA	GIRL	PRIMI	47	87	9	69	22
14	B/O RAJKUMARI KUMAR	2.74	AGA	GIRL	MULTI	39	99	10	67	20
15	B/O USHA THANGAM	2.58	SGA	BOY	MULTI	45	102	8	62	21
16	B/O RADHA UDHAYASANKAR	2.64	SGA	GIRL	PRIMI	47	100	9	66	26
17	B/O PAVITHRA NAGARAJ	2.96	SGA	BOY	MULTI	48	103	6	61	25
18	B/O DHIVYA BHARATH	2.65	SGA	GIRL	MULTI	42	100	9	68	24
19	B/O MENAKA MANIKANDAN	2.69	SGA	BOY	PRIMI	40	94	7	72	26
20	B/O RADHA JAGANATHAN	2.79	AGA	GIRL	PRIMI	36	92	8	60	28
21	B/O POONGODI NAGARAJ	3.42	AGA	BOY	PRIMI	38	97	7	68	21
22	B/O PRIYA KARTHIK	2.85	SGA	BOY	MULTI	47	95	9	65	20
23	B/O JOTHI SANKAR	3.45	AGA	GIRL	MULTI	40	98	10	63	29

24	B/O GEETHA BALAJI	3.6	AGA	BOY	MULTI	44	92	8	68	23
25	B/O JESSI CORAL	2.64	SGA	BOY	PRIMI	42	90	9	66	22
26	B/O FOHINI NAGARAJ	2.74	SGA	GIRL	MULTI	52	100	7	69	20
27	B/O VENDAMANI PRASANTH	3.11	AGA	BOY	MULTI	46	94	6	60	19
28	B/O DHANALAKSHMI VINAI	3.25	AGA	GIRL	PRIMI	39	92	9	58	26
29	B/O RAMYA SANTHOSH	2.94	AGA	BOY	MULTI	36	97	8	66	25
30	B/O SANGEETHA LOGESH	2.86	AGA	BOY	MULTI	39	95	6	68	21
31	B/O JAMUNA BALA	2.68	AGA	GIRL	PRIMI	37	94	8	69	24
32	B/O SARASHWATHY NAVEEN	2.73	SGA	GIRL	MULTI	42	93	5	71	22
33	B/O MOHANA MATHI	2.93	AGA	BOY	MULTI	43	88	5	66	27
34	B/O SALOMI ALEX	2.76	SGA	BOY	PRIMI	49	87	9	62	25
35	B/O JOTHI KANI PRASANTH	3.51	AGA	BOY	MULTI	50	96	8	61	23
36	B/O GOMATHY ASHOK	3.64	AGA	BOY	PRIMI	38	95	9	60	24
37	B/O DEEPIKA SARAVANAN	2.52	AGA	GIRL	PRIMI	36	90	7	70	22
38	B/O INDHU RAGHU	2.56	AGA	GIRL	PRIMI	39	98	6	62	21
39	B/O UMAMAHWSHWARI GURU	2.62	SGA	BOY	MULTI	42	93	7	66	26
40	B/O MONISHA CHANDRU	2.94	SGA	BOY	MULTI	47	97	8	65	25
41	B/O TAMILSELVI PRAKASH	2.67	AGA	BOY	PRIMI	43	92	9	61	22
42	B/O SABIYA FAIZAL	2.68	SGA	GIRL	MULTI	41	90	8	60	24
43	B/O VANDANA BALAJI	2.63	AGA	GIRL	PRIMI	38	88	8	70	27
44	B/O BLESSY SURESH	2.78	AGA	GIRL	MULTI	37	92	6	66	26
45	B/O SAKUNDALA AJAY	2.64	AGA	GIRL	MULTI	32	94	7	67	25
46	B/O ANANDHI ADIYAMAN	2.94	AGA	GIRL	MULTI	39	93	8	62	21
47	B/O RADHA RAVICHANDRAN	3.14	AGA	GIRL	PRIMI	49	92	9	60	20
48	B/O BHUVANESHWARI SANTHOSH	2.65	SGA	GIRL	MULTI	51	86	7	62	24
49	B/O DHIVYA SREENI	3.45	AGA	GIRL	MULTI	36	99	9	68	22

50	B/O KAVITHA SATHYAN	3.65	AGA	GIRL	MULTI	39	89	8	59	24
51	B/O SUNDRAMBAL SUBRAMANI	2.21	SGA	BOY	MULTI	62	98	13	68	24
52	B/O SANTHI RAGHU	2.12	AGA	GIRL	PRIMI	66	103	15	69	26
53	B/O LAKSHMI SELVARAJ	2.38	SGA	BOY	MULTI	70	102	14	58	22
54	B/O ANJALI JORDAN	2.38	AGA	BOY	PRIMI	50	105	15	70	25
55	B/O THENMOZHI MAHESH	2.19	AGA	GIRL	PRIMI	55	86	12	72	24
56	B/O SUDHA PRAKASH	2.09	AGA	GIRL	MULTI	54	95	10	68	26
57	B/O JAYA MOHAN	2.08	AGA	BOY	MULTI	59	90	11	60	27
58	B/O LAVANYA SURESH	2.37	AGA	GIRL	MULTI	55	92	11	62	21
59	B/O RANJITHA KUMAR	2.16	SGA	BOY	MULTI	72	106	14	68	26
60	B/O MYTHILI	2.46	AGA	BOY	MULTI	59	92	12	74	25
61	B/O SELVI	2.3	SGA	GIRL	PRIMI	74	106	11	66	26
62	B/O SOWMYA	2.16	AGA	GIRL	MULTI	72	100	13	70	26
63	B/O ANITHA	2.05	SGA	BOY	PRIMI	68	96	15	74	24
64	B/O RAJKUMARI KUMAR	2.43	AGA	GIRL	MULTI	60	94	12	76	25
65	B/O KAVEERI	2.34	SGA	BOY	MULTI	66	95	13	74	22
66	B/O NIKITHA	2.31	AGA	GIRL	MULTI	58	94	15	70	20
67	B/O AMBHIKA	2.01	AGA	GIRL	MULTI	57	96	14	65	26
68	B/O PADMAVATHY	2	AGA	BOY	PRIMI	65	95	11	62	25
69	B/O AMUL	1.97	AGA	GIRL	PRIMI	60	106	10	66	24
70	B/O LATHA VIJAYKUMAR	2.39	AGA	BOY	MULTI	62	105	12	74	26
71	B/O SHALINI	2.4	SGA	GIRL	MULTI	61	101	12	60	28
72	B/O REENA	1.86	AGA	BOY	PRIMI	59	98	14	68	24
73	B/O GANGA DEVI	2.03	AGA	GIRL	MULTI	74	107	11	65	23
74	B/O MICHEL RANI	2.35	AGA	BOY	MULTI	69	100	15	67	22
75	B/O DHANALAKSHMI VINAI	2.14	AGA	GIRL	MULTI	64	96	16	69	26

76	B/O SARANYA	2.35	AGA	GIRL	PRIMI	66	92	12	75	21
77	B/O MAKESHWARI	2.41	AGA	BOY	MULTI	58	90	14	60	20
78	B/O SARALA	2.12	SGA	GIRL	MULTI	62	94	12	68	26
79	B/O SATHYA SENTHIL	2.35	AGA	BOY	MULTI	66	100	11	70	24
80	B/O SELVI MANIKANDAN	2.15	AGA	GIRL	MULTI	54	96	12	75	23
81	B/O RUBY GANDHI	2.3	AGA	GIRL	MULTI	62	96	10	72	25
82	B/O SANGEETHA SARAN	2.4	SGA	GIRL	MULTI	76	105	16	60	26
83	B/O PUSHPA LOGESH	2.35	SGA	BOY	PRIMI	72	98	15	66	22
84	B/O SALSA KAMAL	2.15	AGA	GIRL	MULTI	60	96	12	68	23
85	B/O PAVITHRA DEVI KARTHI	2.34	AGA	BOY	MULTI	68	102	14	72	26
86	B/O VIDHYA MAHESH	2	AGA	BOY	PRIMI	64	104	11	74	27
87	B/O USHA RANI	2.46	SGA	GIRL	MULTI	70	105	15	60	22
88	B/O JANANI	1.95	AGA	BOY	PRIMI	58	92	13	65	29
89	B/O SAI VAISHNAVI	1.99	AGA	GIRL	MULTI	56	88	12	66	21
90	B/O ROSHINI	2.36	AGA	BOY	MULTI	50	89	11	70	24
91	B/O PARAMESHWARI	2.22	SGA	GIRL	MULTI	62	102	10	72	25
92	B/O BANU	2.1	SGA	GIRL	MULTI	66	0	13	75	27
93	B/O KAVITHA ANTONY	2.35	AGA	BOY	PRIMI	68	92	15	65	26
94	B/O LAVANYA CHANDRU	2.14	AGA	GIRL	MULTI	56	96	10	56	26
95	B/O SINDHU	2.22	AGA	BOY	MULTI	66	94	13	52	28
96	B/O MONIKA	2.35	AGA	BOY	MULTI	58	100	12	68	25
97	B/O SINDHUJA	2.05	AGA	BOY	MULTI	64	98	14	69	22
98	B/O JAYAMALA	2.35	SGA	BOY	MULTI	68	95	13	66	23
99	B/O DHIVYA JAGAN	2.24	SGA	BOY	MULTI	70	99	14	72	22
100	B/O PREETHI	2.35	AGA	GIRL	PRIMI	54	86	10	70	26